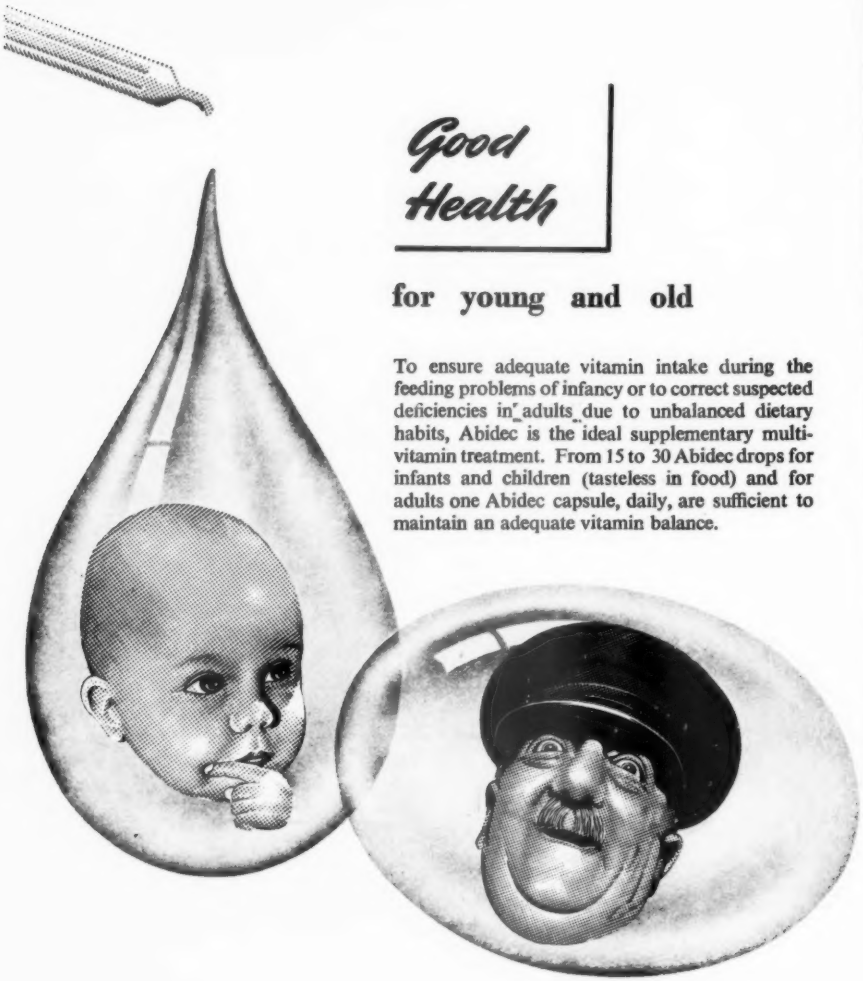
VOLUME 47 NUMBER 1 JANUARY 1954

DOES NOT CIRCULATE

PROCEEDINGS
of the
ROYAL
SOCIETY OF MEDICINE

UNIVERSITY OF MICHIGAN
MAR -3 1954
MEDICAL LIBRARY

Published for
THE ROYAL SOCIETY OF MEDICINE, 1 WIMPOLE STREET, LONDON, W.1
by
H. K. LEWIS & Co. LTD., 136 GOWER STREET, LONDON, W.C.1
In U.S.A., GRUNE & STRATTON, INC., 381, FOURTH AVENUE, NEW YORK CITY
Monthly, 10s. 6d. net Annual Subscription, £6 6s. in the British Commonwealth, $19.00 in the U.S.A.
All rights reserved



Good Health

for young and old

To ensure adequate vitamin intake during the feeding problems of infancy or to correct suspected deficiencies in adults due to unbalanced dietary habits, Abidec is the ideal supplementary multi-vitamin treatment. From 15 to 30 Abidec drops for infants and children (tasteless in food) and for adults one Abidec capsule, daily, are sufficient to maintain an adequate vitamin balance.

Abidec

- *Capsules — bottles of 30 and 250*
- *Drops — dropper-bottles of 10 and 50 c.c.*

PARKE, DAVIS & COMPANY, LIMITED *Inc. U.S.A.*
HOUNSLOW, MIDDLESEX Telephone : Hounslow 2361

PROCEEDINGS *of the* ROYAL SOCIETY OF MEDICINE

ISSUED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS

SIR HENEAGE OGILVIE E. C. WARNER

EDITOR

J. M. BROWNE KUTSCHBACH

ROBERT COPE (Anæsthetics)
FRANCES GARDNER (Clinical)
J. B. BROOKSBY (Comparative Medicine)
D. I. WILLIAMS (Dermatology)
E. F. SCOWEN (Endocrinology)
IAN TAYLOR (Epidem. and Preventive Med.)
A. C. WHITE (Exper. Med. & Therap.)
L. CARLYLE LYON (General Practice)
H. M. SINCLAIR (History of Medicine)
W. A. MILL (Laryngology)
PHILIP ELLMAN (Medicine)
HELEN DIMSDALE (Neurology)
LESLIE WILLIAMS (Obstetrics and Gynæcology)
B. W. FICKLING (Odontology)
FREDERICK RIDLEY (Ophthalmology)
R. C. F. CATTERALL (Orthopædics)
R. SCOTT STEVENSON (Otology)
D. MacCARTHY (Pædiatrics)
F. R. SELBIE (Pathology)
W. S. TEGNER (Physical Medicine)
RONALD W. RAVEN (Proctology)
GERALD GARMANY (Psychiatry)
F. CAMPBELL GOLDING(Radiology)
D. H. PATEY (Surgery)
Surg. Cdr. J. L. S. COULTER (United Services)
A. CLIFFORD MORSON (Urology)

SECRETARY OF THE ROYAL SOCIETY OF MEDICINE

R. T. HEWITT

All communications concerning Editorial Business should be addressed to
THE HONORARY EDITORS, 1, WIMPOLE STREET, LONDON, W.1 (Tel.: LANGHAM 2070)

A New Sandoz Hypnotic and Sedative . . .

PLEXONAL

The combination of sub-threshold doses of 3 barbiturates and of hyoscine and dihydroergotamine is a new solution to the difficult problem of inducing sleep and general sedation without any side or after effects.

Composition

Each tablet of Plexonal contains
45 mg. barbitone sodium,
15 mg. phenobarbitone sodium,
25 mg. sodium isobutylallylbarbiturate,
0·08 mg. hyoscine hydrochloride,
0·16 mg. dihydroergotamine methanesulphonate.

Dosage

One to three tablets as required.

Packages

Tubes of 20 and 200 tablets.

Literature available on request

SANDOZ

SANDOZ PRODUCTS LIMITED

134, Wigmore Street, London, W.1.

HYDRO CORTISONE

MADE IN ENGLAND

AND

CORTISONE

MADE IN ENGLAND

ROUSSEL

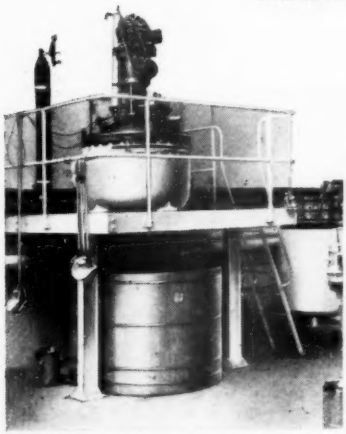
HYDROCORTISONE ACETATE, 25 mg. per cc.; 5 cc. suspension

CORTISONE TABLETS. 5 mg. & 25 mg. Cortisone Acetate: bottles of 20

INJECTION, 25 mg. of Cortisone Acetate per cc.; 10 cc. vials

EYE DROPS containing 1% Cortisone Acetate; 3 cc. dropper bottles

EYE OINTMENT containing 1% Cortisone Acetate; Tubes of 3 G.

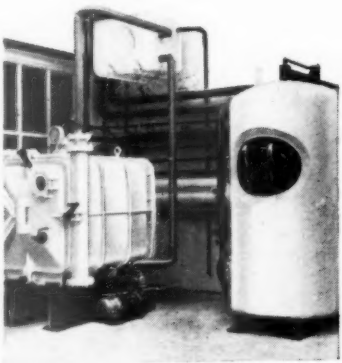


UNITED KINGDOM

We regret that we are not permitted to accept direct orders for the home market for Hydrocortisone and Cortisone, since they are distributed exclusively by the Ministry of Health.

EIRE AND EXPORT

Ample supplies are available for Eire and Export markets; enquiries are welcome.



ROUSSEL LABORATORIES LTD., 847 HARROW ROAD, LONDON, N.W.10. LADBROKE 3608

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Vol. 47 No. 1 January 1954

CONTENTS

	Whole Proceedings Page
The Royal Society of Medicine Wellcome Research Library. Official Opening	1
Section of Orthopædics	
Infected Traumatic Epidermoid Cysts, the Result of Rubbing by an Artificial Limb.—LEON GILLIS, M.B.E., M.Ch.(Orth.), F.R.C.S., F.R.C.S.Ed.	9
Hand-Schüller-Christian Disease Treated with Cortisone.—ROBERT H. SEWELL, Ch.M., F.R.C.S., F.R.C.S.Ed.	10
Acrylic Replacement of Painful Osteomyelitic Femoral Amputation Stump.—A. C. BINGOLD, F.R.C.S.	11
Fracture Separation of Upper Humeral Epiphysis.—DAVID L. EVANS, F.R.C.S. ..	13
Calcification Round the Hips in Paraplegia (Three Cases).—J. C. MCNEUR, F.R.C.S., F.R.A.C.S.	14
Two Cases of Pseudo-Madelung's Deformity.—N. A. STEPHENS, M.B., F.R.C.S., for H. L-C. WOOD, M.S., F.R.C.S.	16
Recurrent Dislocation of Left Elbow of Ten Years' Duration Treated by Kapel's Operation.—F. E. WEALE, M.B., B.S., for H. E. HARDING, F.R.C.S.	18
Clinical Section	
Industrial Raynaud's Phenomenon with Gangrene.—ANDREW M. DESMOND, F.R.C.S.	19
Recurrent Hyperthyroidism.—SELWYN TAYLOR, M.Ch.	20
Prostatic Carcinoma with Pulmonary Metastases: Spontaneous Remission.—H.-J. B. GALBRAITH, M.D., M.R.C.P. (for N. C. OSWALD, M.D., F.R.C.P.) ..	21
Section of Comparative Medicine	
Control of Livestock Diseases in Britain: Some Reflections on the Present Situation. President's Address by Professor T. J. BOSWORTH, M.A., B.Sc., M.R.C.V.S. ..	23

Continued overleaf

The new

PENICILLIN COMPOUND

NO NEED TO PREPARE A SUSPENSION · READY-TO-USE · NO REFRIGERATION NECESSARY

STABILITY: Full potency in aqueous suspension is retained for two years at room temperature — ideal for use in the patient's home.

READY-TO-USE: No tedious mixing required: the patient merely pours out the specified dose after shaking the bottle.

ORAL THERAPY: Provides substantial blood levels without injection in the systemic treatment of mild and moderately severe infections due to penicillin sensitive organisms.

VERY PALATABLE: The aqueous syrup suspension is readily accepted by children and adults.

300,000 *units of Penicillin to each large teaspoonful* (5 *c.c.*)
Supplied in bottles of 60 c.c.

'PENIDURAL'
Trade Mark
Oral Suspension

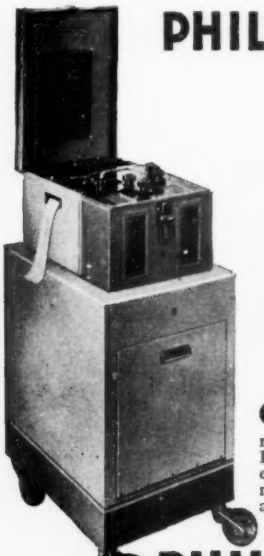
JOHN WYETH & BROTHER LTD., CLIFTON HOUSE, EUSTON RD., LONDON, N.W.1 Wyeth

CONTENTS (*continued*)

	Whole Proceedings Page
Section of Urology	
October 22, 1953	
Malignant Cachexia.—President's Address by HUGH DONOVAN, M.B., F.R.C.S., F.R.C.S.Ed.	27
November 26, 1953	
List of Cases and Specimens shown	32
Section of Anæsthetics	
An Anæsthetist Abroad [*Abridged*].—President's Address by Professor R. R. MACINTOSH, M.A., D.M., F.R.C.S.Ed., F.F.A.R.C.S., D.A.	33
Section of Odontology	
The Microbe Hunters.—President's Address by ARTHUR BULLEID, F.D.S., L.R.C.P., M.R.C.S.	37
Section of Psychiatry	
Moral Responsibility and the Law.—President's Address by E. B. STRAUSS, M.A., D.M., F.R.C.P.	41
Book Received for Review. Books Recently Presented and Placed in the Society's Library	48
Section of Physical Medicine	
DISCUSSION ON SPONDYLOSIS	49
Section of Experimental Medicine and Therapeutics	
DISCUSSION ON THE SURVIVAL OF TISSUES AT LOW TEMPERATURES	57
Section of Epidemiology and Preventive Medicine	
The Epidemic of Poliomyelitis in Copenhagen, 1952.—Professor H. C. A. LASSEN	67
The Anæsthetist's Viewpoint on the Treatment of Respiratory Complications in Poliomyelitis During the Epidemic in Copenhagen, 1952.—Dr. BJØRN IBSEN	72

N.B.—The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Copyright: The Society holds the copyright of all matter accepted for publication in the *Proceedings*. Requests for subsequent publication elsewhere should be made to the Honorary Editors. All papers, &c., presented at meetings (other than those which have been previously published) are held to be subject to the Society's copyright until a decision in regard to their publication has been made.



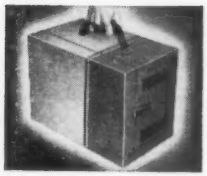
PHILIPS

Cardioluxe

DIRECT-WRITING

Single Channel

ELECTROCARDIOGRAPH



TRULY PORTABLE:
Weight, complete with all accessories, ***only 31 lbs.***

ONE of the most outstanding instrument developments of recent years, the "Cardioluxe" Direct-Writing Electrocardiograph enables physicians to record all modern electrocardiographic leads accurately and instantaneously.

The extreme fidelity of this instrument, brought about by built-in standards of high accuracy, is such that it does not have to be compared with the so-called "standard" photographic apparatus. Complete freedom from interference guaranteed under all conditions. Write for full details.

PHILIPS ELECTRICAL LTD.

ELECTRO-MEDICAL APPARATUS · X-RAY EQUIPMENT FOR ALL PURPOSES · LAMPS & LIGHTING EQUIPMENT
RADIO & TELEVISION RECEIVERS · SOUND AMPLIFYING INSTALLATIONS

ELECTRO-MEDICAL DEPARTMENT, PHILIPS ELECTRICAL LIMITED, CENTURY HOUSE, SHAFTESBURY AVENUE, LONDON, W.C.2
(XF915C REV.)

The Royal Society of Medicine Wellcome Research Library

OFFICIAL OPENING

THE Official Opening of the Wellcome Research Library took place on Friday, December 4, 1953. The opening ceremony was performed by the Rt. Hon. Lord Woolton, in the absence of Lord Salisbury who was prevented from attending by indisposition. Sir Francis Walshe, President of the Society, was in the Chair, supported by the Rt. Hon. Lord Webb-Johnson and Sir Henry Dale. The company of more than 300 included the Chairman of the Wellcome Foundation (M. W. Perrin, Esq., C.B.E.), the Members of the Trust, and representatives of the Ministry of Health, the University of London, the Medical Research Council, and of the various Medical Societies.

A VIEW OF THE SOCIETY'S HOUSE FROM THE SOUTH WEST

This photograph shows the floor which has been added to the top of the building. The Architect for the original building and also for the extension was Mr. J. J. Joass, F.R.I.B.A., who died in 1952 while the work was still in progress. Mr. Lesslie K. Watson, M.A., F.R.I.B.A., who became associated with Mr. Joass a year earlier, was responsible for the completion of the work. The general contractors were Messrs. Trollope & Colls.

The President: My first duty is to welcome those assembled and my second is to introduce Lord Woolton, who has so kindly come at short notice to open the new Library. We are most grateful to him for doing this for us. I hope he will not feel that we have invited him here upon a slight occasion, for indeed we deem it one of some importance not only in the history of the Society but in that of Medicine in this country and in the Commonwealth. This extension of our Library we owe to the foresight and generosity of the Wellcome Trust. Without their support its provision would have been impossible. The Royal Society of Medicine is a wholly academic body and serves every branch of Medicine. It provides a meeting place for the discussion of Medicine in all its aspects and a centre where experts of every kind may place their knowledge before their professional brethren. It might well be argued that the provision and maintenance of the finest medical library in Europe would of itself alone more than justify the existence of this Society, for it is quite a remarkable achievement that a relatively small body of private persons, never more than a few thousand strong, the Fellows of this Society, should have built up a library of over a quarter of a million volumes and have provided for its maintenance, growth and services out of their own resources.

A Library such as this does not spring up in a day. Like a tree it grows, demanding ever more space and sustenance from the soil in which it is rooted. Timely, then, was the munificent gift of £125,000 which we have received from the Wellcome Trust, and I take this first public occasion on behalf of the Society to thank the Trustees most warmly for their generosity. Our special thanks are due to their Chairman, Sir Henry Dale, himself a former President and a very old friend of this Society, and of its Library, for his long-standing and most practical interest in their welfare.

It is not necessary to remind this audience how vital an instrument is a library in the growth and dissemination of knowledge. It is because we regard our own as a great national asset that we have invited Lord Woolton to declare open the Wellcome Research Library, but before I call upon Sir Henry Dale to tell you briefly some of the story of our Library I should like to say to this gathering that our best thanks are due also to the Chairman of the Building Committee, Lord Webb-Johnson, my illustrious predecessor in the Presidency of this Society. It was during his term of office that the enterprise took shape. He has watched over its growth with paternal care. Our thanks are also due to our Architect, Mr. Lesslie Watson and to all who in whatever capacity have borne a share in producing this beautiful addition to our Library, and it would not be right to let this occasion pass without expressing our indebtedness to our devoted and efficient staff, to whom every user of the Library has occasion to be grateful. (*Applause.*)

Sir Henry Dale: I am grateful to you, Mr. President, for giving me this opportunity of telling Lord Woolton and this distinguished company something of the history of this enterprise. All those who have been concerned at any stage with the plan for providing this Society with a much-needed extension of accommodation for its Library are very grateful to Lord Woolton for coming to-day to celebrate with us the completion of that project and for showing his interest in what has been achieved. I know Lord Woolton well enough in other connexions to say that it is characteristic of him to be ready at any time to sacrifice private convenience to do a public service or a personal kindness. We are very sad, of course, that illness has prevented Lord Salisbury from being here in his official capacity, but we are all the more grateful to Lord Woolton, himself a former Lord President of the Council, for coming at short notice to take his place.

It appears that the architect's original design for this building had planned to give it from the outset four storeys, but that some financial stringency at the time it was built—1911—induced the Officers and Council of that day to adopt what must have seemed to them a cautious and conservative policy. They decided to have three floors only, and a flat roof; and they appear to have instructed the architect to make the building strong enough to enable the fourth floor to be added if it should ever be required. The information available suggests that by this curtailment they may have made a temporary saving of something like £5,000 on the cost of the whole four-storeyed building, if it had been completed at that time. We now, of course, have the ungenerous privilege of being wise long after the event.

The Officers and Council of those days cannot have been ambitious in their forecasts of the probable growth of the Society in numbers, or of the eventual demands of its Library for accommodation. The Society had been formed, only a few years earlier, by the fusion of a number of specialist Societies, with the old Royal Medical and Chirurgical Society of London as their co-ordinating centre and nucleus. I suppose that I must now be one of a relatively small number of survivors from the original membership of the new Society. The Officers and Council clearly did not envisage at that early stage a policy which was to give the Library the position of central importance in the Society's services which it has now attained—services which are rendered first to its own Fellows but also on occasion to a wider constituency of medical and scientific men. They had, indeed, inherited from the

Medical and Chirurgical Society—the old Society founded about 150 years ago—a Library of great value, largely because of its complete series of the most important medical journals which were then in existence; but that represented, of course, only a small proportion of those which are in existence now. The Society's plans included, no doubt, a maintenance of the subscriptions to journals which it had thus inherited and such purchases of important new medical books as might be necessary to keep the Library reasonably up to date in accordance with their ideas. They knew that the old Medical and Chirurgical Society had been accumulating its Library for, perhaps, 100 years, and they may have imagined that the rate of progress would be roughly the same in the next 100, so that they ought to provide twice as much space, perhaps, as the Medical and Chirurgical Library had required.

The platform party at the Opening Ceremony.

Left to right: Lord Woolton, Sir Francis Walshe, Sir Henry Dale, Lord Webb-Johnson.

A review of the situation ten years later, however, involving some very vigorous discussion, made it evident how sadly this policy had fallen short of providing what, by that time, had come to be regarded as a necessary standard of comprehensiveness, for the working Library of a Society which was beginning to see more clearly its function, as a centre of meeting for medical men concerned with the advancement of medical knowledge by research, communication and discussion.

After the experience of the First World War it was evident that a new spirit was stirring in medical circles, bringing medical knowledge and its advancement into an ever closer alignment, for the first time in history, with the main current of the progressive experimental sciences. The movement was widespread, and in this country was undoubtedly promoted by the activities of the Medical Research Council, for which you, Lord Woolton, have had a responsibility as Minister in more than one Government.

The Fellows of this Society in 1921 made it abundantly clear to their Officers and Council that the majority desired a fundamental reapportionment of the Society's expenditure, so as to enable this medical Library to be made the best in this country, and probably the best in Europe. The adoption of that revised policy in 1921, though nobody can since have doubted its necessity, had

made it, in fact, inevitable that the accommodation originally planned for the Library, spacious though it had doubtless appeared for the needs as then foreseen, would ultimately become so inadequate that the Society would find it completely filled, and books overflowing into every other part of the building where they could be shelved. Nobody, of course, could then have guessed how rapid, with the expansion and specialization of medical knowledge all over the world, and most conspicuously in the United States, would be the multiplication of journals, monographs and other publications, absolutely necessary for such contact with current advances as the Fellows of a Society like this would increasingly require and demand.

Already by 1930 informal discussions had begun concerning the possibility of meeting the visibly growing need, by the completion of the building in accordance with the original plans. A Sub-committee of the Council reported, however, that nothing could be done without a substantial contribution towards the cost from some outside source; and there was none such at that time in view.

Part of the interior of the Wellcome Research Library.

There the matter was left for more than another decade, while the difficulty of housing the Library, without further detriment to the modest amenities which the building provided for the Fellows, continued steadily to increase.

The great influx of new Fellows, and others in the Medical Services of the Allied Armies, who were given access to the Society's facilities during the Second World War, gave rise to a renewed effort towards the completion of the building, mainly to provide additional space for the Library. Under the Presidencies of Sir Archibald Gray and Sir Henry Tidy new plans were drawn for the proposed addition, provisional estimates of the cost were obtained, and an appeal was made to the Fellows for subscriptions to a Building Fund, to enable the work to be undertaken. The estimate

at that time, however, was already over £50,000 and the appeal raised only between £2,000 and £3,000.

When I took Office as President in October 1948 the tide of wartime emergency and improvisation had receded, but the finances of the Society, under conditions of restored normal activity, were in a state to cause serious anxiety. The Society had very small endowments—it always has had—and its mounting expenditure had to be met, substantially, from the Fellows' subscriptions. Early in my term of Office it became, accordingly, my unpleasant duty to persuade the Fellows to submit to the raising of the rate of subscription, as the only way to keep the Society solvent; and I shall never cease to be grateful for the generous response that was forthcoming from the Fellows, with no more than formal resistance. That being settled, it was possible to look again at the plan for completing this building with Mr. Geoffrey Edwards, then the Secretary, and Mr. J. Joass, the veteran Architect of the building, both of whom had been through all the stages of the earlier discussions. We were, of course, in a period of steeply rising costs, and we had to call for fresh estimates for the provision of the fourth floor and the other work involved. These new estimates showed that the cost had now mounted to £88,000. With that figure in mind, I went to my colleagues, the Wellcome Trustees, who, after considering it with their habitual care, found the project compatible with the terms defining the objects on which the Trust is entitled to spend its resources. They had already given £80,000—since increased to £100,000—to the Royal College of Surgeons for the construction and equipment of a new museum, as part of a building of which the Memorial Stone was laid by Her Majesty The Queen last May. They decided to offer £80,000 to the Royal Society of Medicine, for the new building and re-equipment involved in the provision of the much-needed addition to the Society's Library accommodation. I had the pleasure of transmitting this offer to the Council in October 1950, when the Society was under the Presidency of my distinguished successor, Lord Webb-Johnson. The offer was accepted and I became a member of the new Building Committee under Lord Webb-Johnson who, as its Chairman during his Presidency and since, has devoted a major part of his time to this enterprise and has taken the most watchful care of all its details. The Society is greatly indebted to Lord Webb-Johnson for his part in the successful completion of this project, to which to-day's Ceremony gives authoritative recognition, on behalf of Her Majesty's Government.

It would take far too long to mention all the difficulties encountered and surmounted. In May 1952, Mr. Joass died at an advanced age. He had a natural and jealous pride in his own plans and ideas, still ready to burst into flame under criticism, until the final illness overtook him. I think that we should make a gesture of acknowledgment of our gratitude for his long service to this project; and you will be the more ready to do this, when you all see the austere beauty of the new Library which he designed, and the new fourth floor, which some of you have already seen at luncheon to-day. Fortunately Mr. Lesslie Watson, who had worked in close association with Mr. Joass, took over the responsibility of seeing the work completed in accordance with the accepted plans, and of supplementing these when necessary. He, in turn, has earned our sincere gratitude for the smoothness of the transition.

You can see in this Barnes Hall two square pillars on either side. These enclose two massive steel stanchions running right up from the foundations, through this ground floor and all the floors of the building, to provide support for a framework of steel girders which, in turn, supports the new fourth storey, in compliance with modern structural requirements. The whole of the building operations, including the insertion of these formidable supports for the new floor, right through the existing building, were carried out without any abnormal interruption of the meetings of the Society and its numerous Sections, or of the Fellows' use of the Library, or, I may add, even of the serving of light luncheons to Fellows. That achievement reflects the greatest credit on all concerned—the Officers, the Building Committee, the Architects, the contractors, and, perhaps most of all, on the Society's staff. But inevitably it added materially to the cost. It made the completion of the work very much slower, during a period of steeply rising costs. In one way or another, the Society eventually found itself in difficulty; but the Wellcome Trustees, being apprised of the situation and having studied it with their customary care, agreed to provide, in two successive instalments, a further total sum of £45,000, in addition to their original gift of £80,000. That was rather more than the proverbial extra "ha'porth of tar", but, in any case, the Trustees were quite determined that the ship should not be spoilt for the lack of it.

To complete the tale I should mention that the Wellcome Trustees were further concerned to ensure that the advantages of the new Library, and of the Society's meetings and discussions, should be open as widely as possible to younger medical graduates who could not yet afford the subscription to the Society's Fellowship, and especially to those from overseas, engaged in London in medical research or in studies for higher degrees. For a term of years, therefore, the Trustees have put at the disposal of the Society an additional annual sum, equivalent to the subscriptions which the Society would otherwise have been obliged to charge for the facilities given to these Wellcome

Associates, of whom three hundred can be elected at any one time. There has been no difficulty in filling the list.

I am sorry that Lord Waverley has had to go, because I should have liked to draw his attention to the fact that a substantial proportion of these Associateships are being awarded to young overseas graduates studying under the British Post-Graduate Medical Federation. I may perhaps add that the Trustees have not found it discouraging to hear from the Librarian that each of these Associates requires about five times as much service from the Library staff as an ordinary Fellow of the Society.

Meanwhile the Fellows of the Society, under the generous lead again of Lord Webb-Johnson, have reopened their Building Fund, which now stands at about £8,000; and this will be devoted to the provision of the additional amenities to be found on the new fourth floor, which do not come within the scope of the expenditure permitted to the Wellcome Trust.

Finally, Sir, I should like to say that we regard Lord Woolton's presence, on this occasion of the opening of our Research Library, as a token of the recognition by Her Majesty's Government of the important part which this Library of the Royal Society of Medicine has come to play in the advancement of medical knowledge in this country. We remember again that Lord Woolton until recently occupied the Ministerial Office which Lord Salisbury now occupies, and which is responsible for the support for medical research by the Government. The Library has become by far the most widely used source of medical literature to workers in medical research and practice in Britain, and its resources, by means of micro-film and photostat, are being made widely available to the Fellows of this Society throughout the Commonwealth and Empire. Nevertheless, as the President has emphasized, this is a private enterprise, built up and maintained, on a basis inherited from the ancient Royal Medical and Chirurgical Society, from what can be spared from the subscriptions of its Fellows—subscriptions which have now been raised, I suspect, to a level above which they cannot go, at least for a long time to come. They are, of course, subject also to ever-increasing demands to meet the Society's inevitably rising expenditure on other services. It is from the results of private enterprise, again, that the Wellcome Trustees have been privileged to provide the means for the large additional accommodation, so urgently needed for the proper housing and effective use of this Library's great and growing wealth of medical books, journals and treatises.

We do not delude ourselves with a belief that we have provided therewith a permanent solution of all the problems concerning its Library, which will face this Society in the future. On the other hand we do not fear that our single contribution, or the cumulative contribution made over the years from the Fellows' subscriptions, will ever be allowed to go to waste. This Library, though it is private property, created by private thrift and enterprise, has acquired something of the status of a national and an imperial possession. We are confident that, whatever happens, its value to the community will not be allowed to be lost, or to diminish. (*Applause.*)

The President: We thank Sir Henry Dale for his brief *résumé* and I should like to point out again how immeasurably indebted this Society is to him and to the Wellcome Trustees. I will now ask Lord Woolton to declare the Library open.

The Right Hon. Lord Woolton: I am here to-day only as a substitute for Lord Salisbury who is suffering from one of those ills which continue to defeat your profession, the common cold. This has thrown on me the responsibility of performing this opening function; I am sure Lord Salisbury would have enjoyed doing it very much.

It gives me great pleasure to be here to-day to see you in your home and to see also this most valuable addition to your Library that comes as a result of the munificent gift of £125,000 from the Wellcome Foundation. Lord Webb-Johnson came to me yesterday afternoon when I was endeavouring, as is my duty, to follow a Debate in the House of Lords on an important question affecting Scotland; with one ear I listened to Lord Webb-Johnson and with the other I listened to the subject before the House. Lord Webb-Johnson reminded me that he and I were graduates at the same University and that it would be very appropriate if I consented to perform this duty in Lord Salisbury's absence. He also put into my hand the complete account of what I ought to say. I took it home and read it with much interest. I am glad to be here for more than one reason. I wanted to come because Sir Henry Dale is so closely concerned with this occasion: when I was Minister of Food I took much advice from him and from others. I will not say that I was completely successful in following his advice all the time, but at any rate I did try, and I do not think the health of the nation suffered under our joint administration. Then I had another helper who came here a great deal and that was the late Sir Jack Drummond. I remember so well coming here one night when Sir Jack Drummond asked me to meet a number of doctors. One of the advantages a Minister of Food enjoys in this

country is that he gets a multitude of advice from a wide range of the public as to how he could conduct his operations, and I remember that night I went away with my head rather bowed as a result of hearing what a number of eminent physicians had told me of my deeds and misdeeds.

There is another reason—a very personal one—which made me glad to come to the Royal Society of Medicine. I owe so much to your profession—in fact I owe to it that I am here at all. Never shall I cease to be grateful for the infinite care and attention that as many as fourteen members of your profession bestowed on me. One of them remarked on the constitutional powers I must possess to have withstood so much advice.

I had, as Sir Henry Dale reminded you, some Ministerial responsibility for the medical profession when I had the honour—and it is a great honour—of occupying what I think is the most enviable position in the Cabinet, that of Lord President of the Council. The Lord President is responsible for scientific research and particularly responsible for the Medical Research Council, and responsible also—though I never went into it too closely—for the General Medical Council. I have come to know something of the history of your great science and anyone who as an amateur has studied it cannot fail to be aware of the magnitude of the achievements of the medical profession and the interest of its history. Certainly we are all indebted to the founders of this Society and to those who, inspired by them, have continued in its tradition.

There is no part of its activities of which this is more true than your Library. The creation of a Medical Library, numbering, I am told, a quarter of a million books, is in itself a gigantic task. It never could have been competently and wisely accomplished in a short space of time. A good library is not something that is suddenly created. It is a growth, and it is due to the far-sighted labours of your predecessors over 150 years, that to-day you are able to assist so large a public. The figures given me seemed so extraordinary that when I came here to-day I questioned them with your President. I am told that you have in the course of the year between 40,000 and 50,000 occupants of your library chairs, and, moreover, there are withdrawals from the Library for members in the provinces to the number of something like 80,000 volumes. The importance of the service which this Library renders to the cause of Medicine and Medical Research is beyond computation. It did not surprise me to hear you say that this is not only a great national library; I think you said with modesty that it is the largest medical library in Europe, and I was told to-day before I came here, by my friend Sir Harold Himsworth, that it was probably the greatest medical library in the western hemisphere. There can be no doubt that it will remain a very proud possession not only of you who are here to-day but of all those who will succeed you.

I was interested to hear Sir Henry Dale describe the financial difficulties of the past. I imagine you are going to face such in the future because scientific research is of steady growth and the output of scientific and medical literature is large and increasing. Apparently you have to add something like 5,000 volumes a year to your Library. That is the expected rate of growth and you may find yourselves before long confronted with the same difficulties as you had before this gift which we honour to-day came your way. I do not know whether the pillars in this hall which conceal the constructional steel stanchions would permit of your rising to still more floors on this building. The problem of the growth of libraries is something of which those of us who are connected with Universities are ever conscious. It is a problem common to all branches of science and of learning. The Government is much concerned that the findings and the records of scientific advance should be made as widely available as possible by means of the adequate services of technical libraries, and the Lord President's office is considering ways of meeting the present specialist library requirements. In the field of medicine you in the Royal Society of Medicine are undoubtedly playing an outstanding part. I realize that if your Library continues to grow, as it inevitably must in order to fulfil its purpose, it will become an increasing strain on your resources. I gather that it is already costing you in the neighbourhood of £25,000 a year and it may well be before long that you will wish to consider some ways of associating yourselves with other more general schemes which Her Majesty's Government has in mind for providing technical literature for scientific specialist workers. It may mean that your facilities can be made more widely available in the endeavour to spread the cost which is becoming so heavy a burden on all branches of scientific work. It seems inevitable that the many interests in this field must come to some agreement to collaborate with one another if the public need and interest is to be served, within the bounds of our financial resources.

I am personally convinced—I do not want to commit anybody else—that the vast project for a national medical library is bound to be extravagant and unduly expensive, and to involve unnecessary overlapping and confusion, and that the alternative lies in the collaboration of which I have spoken. In this field collaboration is better than competition and the Government will welcome the opportunity of discussing these problems with you when you consider the time is ripe. I believe there has been some talk of your acquisition of adjoining premises to meet future needs. I spoke to the Postmaster-General about it and I understand that successive Postmasters-General and Ministers

of Works have been approached on the question. I will not say any more on that subject except that it would not be amiss to ask the Postmaster-General what he was going to do about it.

I now formally open these beautiful rooms. They give one a powerful impression of the services of a library to-day. I congratulate you, Sir, and the Royal Society of Medicine on these additions that you have made and, I congratulate the Trustees of the Wellcome Foundation on the wisdom and the public spirit they have shown in making such generous provision for this purpose. Finally I congratulate my old friend Lord Webb-Johnson on the work he has done and your Honorary Librarian, Mr. H. J. Seddon, on the new premises which are now at his disposal. It is indeed with pleasure that I declare the Wellcome Research Library open. (*Applause.*)

The Right Hon. Lord Webb-Johnson: I am deeply grateful for this opportunity to express the thanks of the Society and also of the Trustees of the Wellcome Foundation to Lord Woolton for his presence here to-day. It would not be fitting if I did not express my regret that Lord Salisbury is ill and in this regret Lord Woolton will join with me, but Lord Woolton comes here into an assembly where he is always welcome for his own sake whatever Office he may hold. We shall ever be appreciative and grateful to Lord Woolton for his services during the War when he literally saved the life of the nation. Not only that, but we are grateful to him for the fact that he is always ready and anxious to learn and we know that if he thought he could do any service, whatever the strain might be upon him, he would be most ready to do it. In this Society and in every medical assembly he is sure of a very warm welcome. We are extremely grateful to him for his speech and on behalf of the Royal Society of Medicine and of the Wellcome Trustees I offer Lord Woolton our warmest thanks. (*Applause*).

The company then adjourned to inspect the new premises.

Section of Orthopædics

President—H. L-C. Wood, M.S., F.R.C.S.

[*October* 6, 1953]

Infected Traumatic Epidermoid Cysts, the Result of Rubbing by an Artificial Limb.—Leon Gillis, M.B.E., M.Ch.(Orth.), F.R.C.S., F.R.C.S.Ed.

E. G., male, aged 50.

This patient has worn an artificial limb on a right above-knee amputation since 1933 and developed an infected focus in the stump twelve months later. Further abscesses appeared, and for the last fifteen years the stump has been discharging constantly, although he has worn the prosthesis at all times.

When seen in June 1953 there was a large area of puckered, scarred skin on the inner side of the stump, with three discharging sinuses, probably communicating by fibrous subcutaneous tracks. Examination of the pus revealed *Staphylococcus aureus* only, and he has been treated up to now by antibiotics, local antiseptics and infra-red rays (Fig. 1). The acute inflammation has subsided, but the problem of limb fitting remains as the stump is at present unsuitable to wear a prosthesis.

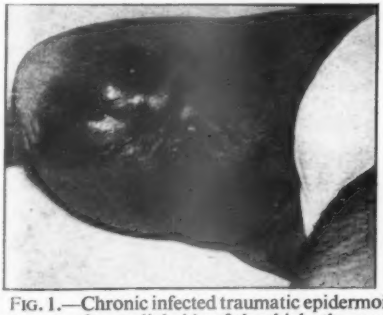


Fig. 1.—Chronic infected traumatic epidermoid cysts over the medial side of the thigh, the result of an unsuitable socket.

Fig. 2.—Excision of an ellipse of skin down to deep fascia. Macroscopic section shows thickened skin with cystic area.

The histological picture can be described under the following headings:

(1) The epidermis becomes invaginated at an early stage.

(2) Large pockets of keratin appear in the sub-epidermal regions.

(3) Cysts are separated close to the surface.

(4) Cysts appear in the deeper tissues (Fig. 2).

(5) The cysts become infected, producing sinuses and there is an inflammatory reaction and giant cells appear around.

The cause of this condition is a poorly fitting artificial limb where the shape and the alignment of the socket are unsuitable for the anatomical configuration of the thigh stump.

Hand-Schüller-Christian Disease Treated with Cortisone.—ROBERT H. SEWELL, Ch.M., F.R.C S., F.R.C.S.Ed.

I. B., female, aged 3 years 10 months.

March 1952: Otorrhœa followed by a limp.

A tender hard swelling of the left femoral metaphysis was found with full range of knee movement (Fig. 1). Exploration revealed a cavity lined with greyish granulation tissue. This was curetted and on section was reported as an eosinophil granuloma. The blood count was normal except for 3% eosinophils. Blood chemistry normal. No diabetes insipidus. No Bence-Jones protein.

Skeletal survey revealed geographical defects in the left temporal region (Fig. 2).

FIG. 1.—X-rays of left femur.

FIG. 2.—Defects in temporal region.

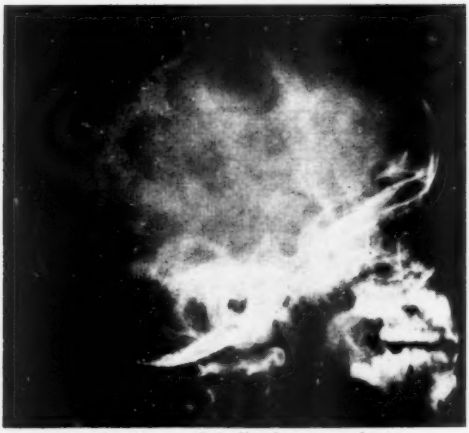


FIG. 3.—X-ray of skull prior to cortisone.

FIG. 4.—X-ray of skull after three months' treatment with cortisone.

Progress.—After curettage the femoral lesion healed. The skull deposits increased in size and number despite X-ray therapy (Fig. 3). New deposits appeared in the mandible, right scapula, right humerus, left clavicle and right ilium. There was exophthalmos on the left.

January 1953: When she had failed to respond to X-ray therapy and her condition was deteriorating she was given intramuscular cortisone 50 mg. daily, later reducing to 37½ and now 25 mg. daily. Her general condition has improved greatly. The exophthalmos has slowly increased. The skull deposits have increased in size but the centres show calcification (Fig. 4). No new deposits have been discovered since cortisone therapy was commenced.

Biopsies

(1) Of original femoral lesion: "Large numbers of mononuclear cells and eosinophils." "Small numbers of foreign body type giant cells are present."

(2) Of skull lesion prior to cortisone: "A fair proportion of the tissue is fibrous in type. Lying in the fibrous stroma are varying sized collections of mononuclear cells. The cytoplasm of the cells appears a little foamy. Numerous eosinophils are scattered among these mononuclear cells."

(3) Of skull lesion after cortisone: "This section is composed mainly of large well-formed foamy cells." "There is a little thin fibrous tissue at one edge." "Eosinophils are completely absent."

Comment

This case showed the histological features of an eosinophil granuloma in the first biopsy with those of Hand-Schüller-Christian disease in the later ones. It supports the theory of Farber (1941) that these conditions are pathologically akin.

A future biopsy may decide whether the central calcification of the skull lesions is evidence of healing or possibly calcification of central necrotic tissue. Whether the clinical improvement with changed radiological features in this case of Hand-Schüller-Christian disease is spontaneous or due to cortisone must, at present, remain uncertain.

I wish to thank Dr. B. Gans for his co-operation in the treatment of this case, and Dr. G. Thomas who reported on the biopsies. Mr. J. Andrews of the Park Hospital, Lewisham, kindly prepared the illustrations.

REFERENCE

FARBER, S. (1941) *Amer. J. Path.*, **17**, 625.

Mr. H. E. Harding said that he could report 3 cases of this condition from his own experience. The first was typical in all the main features, with very marked exophthalmos. There were localized lesions in all cases in the membrane bones. Biopsies showed the characteristic lipo-granulomatous appearance. Radiation treatment had been tried, and during this period—three or four years—only minor changes occurred, whether spontaneously or caused by the radiation he did not know. Irradiation certainly appeared to affect the local lesions.

Acrylic Replacement of Painful Osteomyelitic Femoral Amputation Stump.—A. C. BINGOLD, F.R.C.S.

Seddon and Scales (1949) were the first surgeons to report the construction of a femoral amputation stump in which the femur was replaced by an internal plastic prosthesis. Their patient was suffering from fibrous dysplasia of a femur.

To the author's knowledge the patient reported here is the first to be relieved of pain arising in a mid-thigh amputation stump by a similar operation.

Case Report

History.—A man aged 38 was admitted on 3.11.52 complaining of agonizing pain in his left femoral amputation stump. An attack of osteomyelitis in his left femur at the age of 12 had necessitated many periods of prolonged hospitalization and many operations including drainage of abscesses and sequestrectomies. A resection of 8 in. of femoral shaft followed by an attempted repair of the defect with a fibular graft had eventually led to amputation through the mid-thigh when he was 26 years old. The stump had never been healthy and abscesses had been drained on two occasions. At the age of 28 an artificial limb was fitted, but he discarded it a few months before his admission on account of severe pain which had two elements: (1) phantom-limb pain of two to three years' duration; (2) pain on the inner side of the stump present for the last six or seven months.

On examination.—The patient was greatly distressed and in severe pain. He had a 7 in. left femoral amputation stump with a deeply sulcated terminal and several lateral scars. There were extreme tenderness and hyperæsthesia over the tip and the medial portion of the stump. No neuromata could be felt. Movements were full but with jactitation. There was no fixed deformity.

A radiograph showed a markedly irregular femoral stump containing a piece of metal (Fig. 1).

On the assumption that it was the diseased bone that was causing the pain, treatment, including lumbar sympathectomy, was at first directed to interrupting the sensory and sympathetic pathways but without success. It was therefore decided to replace the bone by an acrylic prosthesis (Fig. 2),

FIG. 1.—Pre-operative radiograph of the stump showing the irregular distal portion, the two spicules below the tip and the piece of metal near the lesser trochanter.

FIG. 3.—The resected bony stump. The arrow points to a small abscess cavity.

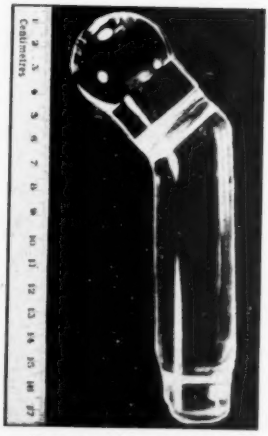


FIG. 2.—The prosthesis.

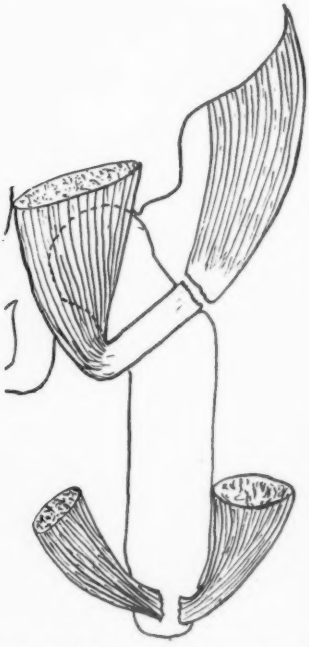


FIG. 4.—Diagram of the muscle attachments to the prosthesis.

FIG. 5.—Stump ten months after the operation.

the dimensions of which were determined by slit radiography. It was fashioned with no trochanters; a channel was provided at the neck-shaft junction and a wide coronal groove at the distal end.

Operation (30.12.52).—A strip of fascia lata was first obtained from the right thigh. Through a lateral incision the left femur was exposed through fibrosed vastus lateralis and filleted out with a diathermy electrode and a few touches of the scalpel. Special care was taken to secure the psoas tendon. The capsule of the hip-joint was opened and the head of the femur was delivered by gentle traction and the whole piece of bone was lifted out of the wound (Fig. 3).

The abnormal findings were: (1) dense scar tissue at the lower end of the stump which spread upwards on the medial side and contained a number of bony spicules, (2) a large neuroma on the sciatic nerve and (3) intense fasciculations of the quadratus femoris and the upper part of the adductor magnus present throughout the operation. The scar tissue and the neuroma were resected. The prosthesis was inserted. The psoas tendon was passed through the tunnel and stitched to the glutei and the tensor fasciæ femoris with strips of fascia lata. The muscles were secured round the shaft of the prosthesis with two circumferential fascial sutures. Distally the ends of the adductors and vastus lateralis were stitched to each other in the groove at the tip of the prosthesis (Fig. 4). The vastus lateralis was closed over the artificial femur. Two glove drains were inserted.

Progress.—The patient's convalescence was marred by bouts of severe pain in the stump, which pain disappeared within one month, and by slow healing of the distal end of the wound. After three months the stump was healed and painless so that the patient was sent to a limb-fitting centre. He wore a pylon at four months and an artificial limb with a double swivel hip-joint six and a half months after his operation.

Ten months after his operation he stated that he had no pain but occasionally felt "pins-and-needles" in the foot of his phantom. On examination his stump was not tender and had a full range of strong active movements (Fig. 5). There was no deformity of the hip-joint. He was walking well on his artificial limb.

Discussion

Consideration of the three abnormal findings in this patient's stump leads us to the following conclusions:

(1) The intense fasciculations of the quadratus femoris and upper part of the adductor magnus were in all probability produced by operative trauma and were of no significance.

(2) The sciatic neuroma was also unimportant: the pain in the stump was felt in the distribution of the obturator nerve, and phantom-limb pain is not usually relieved by resection of a neuroma.

(3) The osteomyelitic femoral stump and the scar tissue round it must be regarded as the cause of this patient's pain, since after their removal the pain disappeared. This conclusion cannot lightly be dismissed, although no previous writers, not even Riddoch (1941) and Falconer (1953), have considered diseased bone and scar tissue a source of pain in stump or phantom.

In spite of the satisfactory short-term result it would be wrong to claim a cure in this case since Lewin and Phillips (1952) have reported a patient whose pain started twenty-seven years after amputation. It is felt that the method is worth further trial.

REFERENCES

Falconer, M. A. (1953) *Brit. med. J.*, i, 299.
Lewin, W., and Phillips, C. G. (1952) *J. Neurol. Psychiat.*, **15**, 143.
Riddoch, G. (1941) *Brain.*, **64**, 197.
Seddon, H. J., and Scales, J. T. (1949) *Lancet*, ii, 795.

Fracture Separation of Upper Humeral Epiphysis.—David L. Evans, F.R.C.S.

D. S., a boy aged 5, was transferred to Westminster Hospital on 30.10.51. One month earlier he had fallen some 14 feet, sustaining a fracture separation of the right upper humeral epiphysis (Fig. 1). Two attempts at closed reduction had been made elsewhere, without improving the position.

Examination revealed the upper end of the humeral shaft projecting under the skin at the point of the shoulder. Movements of this joint were minimal and caused pain. X-ray showed no change in the deformity but much callus formation. No surgical intervention was indicated. He was encouraged to begin moving his shoulder.

Over the past two years movements of this joint have steadily increased, and the clinical and radiological deformity has become less marked.

Examination two years after injury reveals bowing of the upper end of the humerus, with some consequent shortening of the arm. Limitation of movement at the shoulder is only noticeable in abduction.

Fig. 1.—October 1951.

Fig. 2.—September 1952.

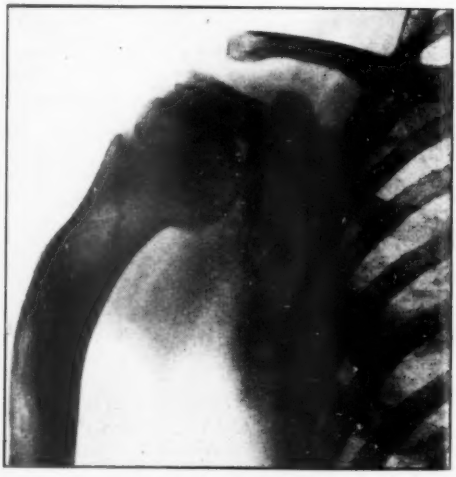


Fig. 3—September 1953.

Serial X-rays (September 1952, Fig. 2, and September 1953, Fig. 3) show the extraordinary degree of remodelling of the upper end of the humerus that has occurred in two years. As the boy is now only aged 7, there is every reason to anticipate an almost normal bone by the time growth ceases.

Calcification Round the Hips in Paraplegia (Three Cases).—J. C. McNeur, F.R.C.S., F.R.A.C.S.

I.—Male, aged 42.

One week following a course of anti-rabies injections he developed transverse myelitis about the level of D.4. Flexion and adduction spasm of the legs was present and he required a suprapubic cystotomy for bladder paralysis. A sacral pressure sore developed. Gradually power and sensation returned, but seven months later it was noticed that both hips were adducted and could be separated only slightly. X-rays taken at this time showed massive calcification about both hip-joints, but worse on the left side (Fig. 1). Only a trace of movement is present in either joint.

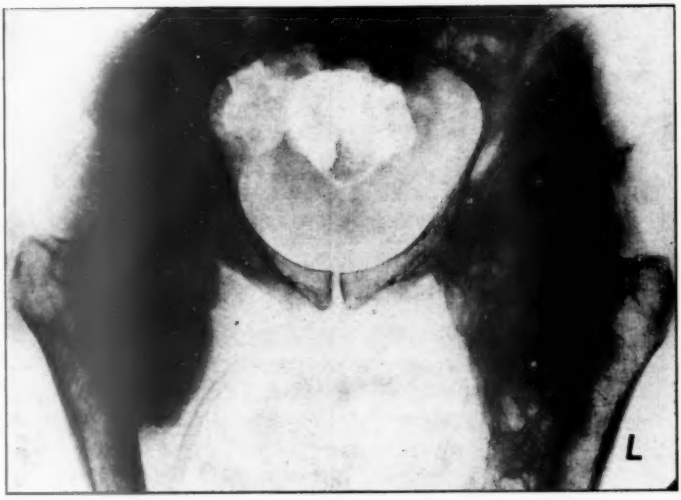


FIG. 1.

II.—Male, aged 34.

Following a fall, with fracture of the spine, he developed paraplegia below D.10 level. Suprapubic cystotomy was required and large pressure areas developed over both great trochanters and sacrum. Severe flexion and adduction spasm of the legs necessitated alcohol injections into the spinal cord. Eighteen months after the injury X-rays showed massive calcification about both hip-joints (Fig. 2) and there was no movement present in either hip.

FIG. 2.

III.—Female, aged 44.

Immediately after thoracolumbar sympathectomy in 1941 for hypertension she developed paraplegia below D.10. There were persistent pressure sores and a sinus over the left ischial tuberosity which remained until 1952. Early in 1953 a small pressure sore developed over the left greater trochanter and from this time the left hip became increasingly stiff. X-rays taken in August 1953 show marked calcification about the left hip-joint, and only slight calcification on the right side

(Fig. 3). The left hip was fixed in a good position for walking, but was in an unsatisfactory position for sitting.

FIG. 3.

DISCUSSION

The combination of spasm and local sepsis appears to be conducive to this type of ossification which is apparently localized to the anterior aspect of the joint. The spastic muscles and contracted capsule on the front of the joint, in being stretched to correct flexion contracture, are submitted to repeated minor trauma, resulting in small foci of hæmorrhage and tearing of fibres of insertion into bone. This may explain why other aspects of the hip are not affected by the same calcifying process.

Cases I and III are alive and well but Case II died of chronic sepsis and amyloid disease three years after the onset of paraplegia. Autopsy disclosed that the ossification was mainly in and replacing the iliacus muscles and that it was entirely over the anterior aspect of the joints.

Two Cases of Pseudo-Madelung's Deformity.—N. A. STEPHENS, M.B., F.R.C.S., for H. L-C. WOOD, M.S., F.R.C.S.

Case I.—E. A., male, aged 18.

History.—When aged 9 he fell and injured the right wrist. At this time X-rays at another hospital showed no fracture. For a few months after this injury symptoms disappeared, but when first seen at King's College Hospital he complained of severe pain and swelling over the inner border of the right wrist.

On examination.—When seen in 1948 he had established radial deviation of the right hand and a marked prominence of the lower end of the ulna, which was tender. X-rays showed a cupped, irregular almost fused radial epiphysis with overgrowth of the lower end of the ulna, the inferior radio-ulnar joint being dislocated (*see* Fig. 1A and B).

Operation (Mr. H. L-C. Wood), 26.8.48.—A subperiosteal resection of one inch of the lower end of the ulna was performed. No attempt at repairing the medial ligament was considered possible.

Progress.—Five years after operation he now has a strong wrist with no obvious clinical deformity. He is engaged in heavy work as a packer, and beyond the fact that his right forearm is 1½ in. shorter than the left, he is conscious of no disability. (Fig. 2 shows the X-rays after four years.)

Case II.—R. P., male, aged 12. (Not illustrated).

History.—This boy fell out of a tree on 5.7.50 when aged 9 and sustained a separation of the right radial epiphysis. Satisfactory reduction was obtained and full union was present after six weeks. A further history of injury to the wrist when aged 3 years was obtained but no X-ray confirmation was obtainable. For the past six months the wrist has become increasingly painful and swollen over the inner side.

On examination.—Radial deviation of the wrist and prominence of the lower end of the ulna are

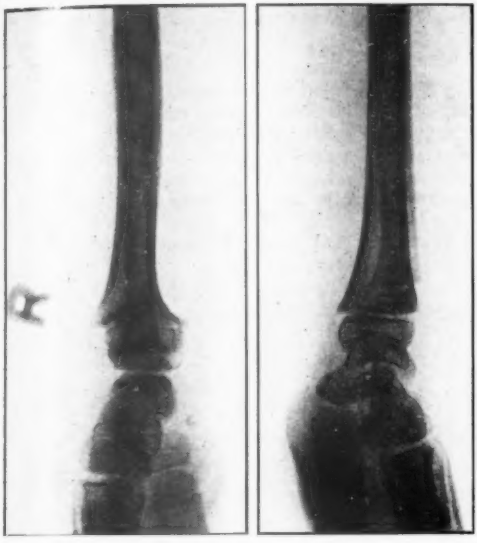


FIG. 1A.

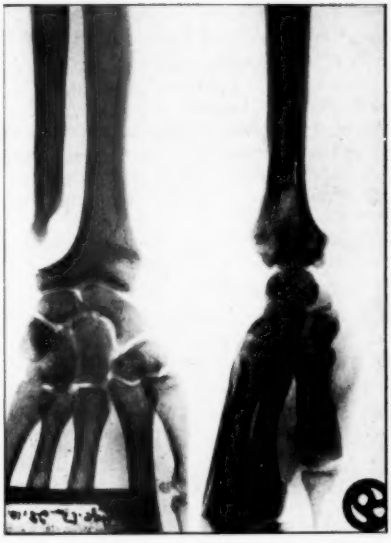
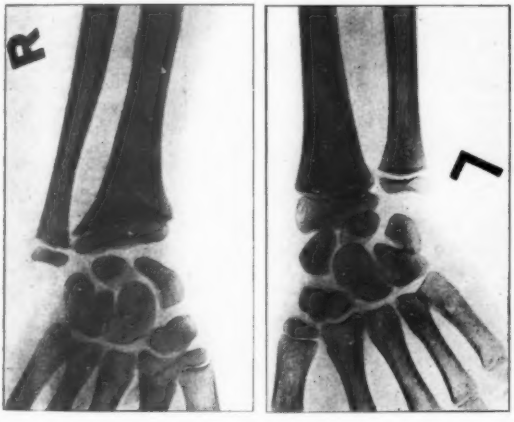


FIG. 2.—Result seen four years after operation.



FIGS. 1A and B.—Comparative views of both wrists showing pseudo-Madelung's deformity.

←FIG. 1B.

marked features, as in the first case. X-rays showed a similar but earlier lesion, with onset of fusion of the rather cupped radial epiphysis, and continued growth of the lower end of the ulna.

DISCUSSION

It was felt that operation in the first case, after the method described by Darrach, had given a good result. An alternative would be to excise the epiphysis and adjacent ulna, as described by Burrows (1937), leaving the ulna head and medial ligament intact, and performing an osteotomy of the lower end of the radius. However, the remaining growth of the radius could not be predicted and further loss of length of the forearm might result as, in both cases, they presented themselves for treatment at an early age.

It would appear that such deformity of the wrist from injury in childhood is unusual, since the last mention of cases of this nature in the English literature was that of Burrows in 1937.

REFERENCE

BURROWS, H. J. (1937) *Proc. R. Soc. Med.*, **30**, 565.

Recurrent Dislocation of Left Elbow of Ten Years' Duration Treated by Kapel's Operation.—F. E. WEALE, M.B., B.S., for H. E. HARDING, F.R.C.S.

T. H. C. S., male, aged 33.

Past history.—First dislocated his left elbow in 1942. It was reduced, and he was free from trouble until 1951. The elbow re-dislocated as he was putting his coat on; this recurred on five occasions, but he was able to reduce it himself without difficulty. No relevant family history.

On examination.—A little fluid was present in the joint, and there was some tenderness above the head of the radius. The X-rays showed a normal olecranon fossa, and a thin flake of bone anterior to the elbow-joint. Manipulation under anæsthesia confirmed the ease with which the joint could be dislocated.

27.2.52: Operation. Elbow approached through anterior and posterior incisions, as described by Kapel (1951), and straps of triceps and biceps secured as shown in Fig. 1.

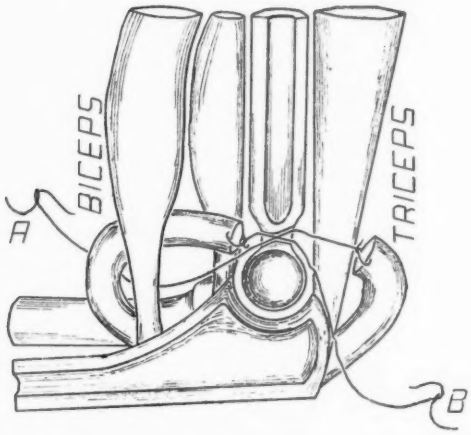


FIG. 1.—Diagram of operation (after Kapel). A, Suture pulling strap of triceps through hole in humerus to coronoid process; B, suture pulling strap of biceps in opposite direction, to be fixed to olecranon process.

6.10.53: The patient works as an ambulance driver and stretcher-bearer. There is no loss in muscular power, no loss in supination-pronation movements and flexion; extension is reduced by about 20 degrees (Fig. 2). His elbow has not dislocated since his operation.

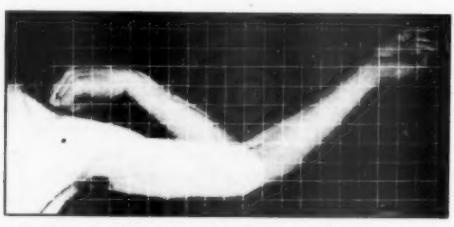


FIG. 2.—Range of movement twenty months after operation.

REFERENCE

KAPEL, O. (1951) *J. Bone Jt. Surg.*, **33A**, 707.

Mr. H. E. Harding said he made no claims for the operation. He had carried it out for lack of anything better and somehow it had worked, since the man was reasonably grateful and had returned to his original employment as an ambulance stretcher-bearer.

Proceedings of the Royal Society of Medicine Vol. 47 19

Clinical Section

President—JAMES L. LIVINGSTONE, M.D., F.R.C.P.

[*October* 9, 1953]

Industrial Raynaud's Phenomenon with Gangrene.—ANDREW M. DESMOND, F.R.C.S.

Gangrene is an uncommon complication in Raynaud's phenomenon and allied syndromes, and usually presents as small ischæmic ulcers of the finger tips. Gangrene in that form of the phenomenon associated with industrial occupations is extremely rare and probably unknown under the age of 50 years.

The case presented is therefore one of unusual interest.

CASE REPORT

A. H., a male labourer aged 50 years, was referred to me on 13.5.53 from the Mayday Hospital with established gangrene of all the digits of the right hand and two of the left.

For many years he had used a roadmender's pneumatic drill but had noticed no untoward effects on his hands. He did not suffer unduly from coldness of his extremities. Early in March 1953 he was using a vibrating drill for one day only on a demolition job, and it did not affect his hands on this occasion. He then started using a club hammer and cold chisel (8–9 in. long) on the same work and towards the end of March noticed that the fingers and thumb of the right (hammer) hand down to the knuckle would go dead white. Also the middle and little fingers of the left (chisel) hand behaved in a similar manner. As soon as he stopped using the hammer the fingers returned to normal, but as soon as he recommenced, the whiteness recurred. After three weeks the tips of all digits of the right hand and the middle and little fingers of the left became ulcerated.

13.4.53: Admitted to the Mayday Hospital; the involved fingers became gangrenous and infected producing a cellulitis and œdema of the right hand and lower forearm.

Investigations.—Wassermann reaction negative.

X-rays: Chest: Normal. Neck: No cervical rib or prefixation. Hands: No bone necrosis of digits. He was given a course of Priscol with no apparent effect.

13.5.53: Transferred to St. James's Hospital.

On admission.—A well-built muscular man.

General examination revealed nothing abnormal except for the sensation of the hands.

Right hand.—Œdema of whole hand and wrist. Thumb, superficial pulp gangrene—dry. Index, black dry gangrene to just proximal to distal interphalangeal joint. Middle, black dry gangrene to distal interphalangeal joint with superadded infection. Ring, similar to index. Little, superficial pulp gangrene.

Left hand.—Middle, dry gangrene of tip. Little, very slight dry gangrene of tip.

Re-X-ray of cervical spine normal. No cervical rib.

19.5.53: Subclavian arteriograms were carried out under general anæsthetic using 70% diodone. Results were inconclusive.

28.5.53: Right cervico-dorsal sympathectomy was performed by the Goetz approach through the bed of the 3rd rib in the axilla. The operation was entirely extrapleural; the chain was cut below the 3rd ganglion, the 2nd and 3rd ganglia were removed and all communications cut.

Post-operative course was uneventful and sweating tests showed a "complete" sympathectomy. The swelling and infection of the fingers and hand subsided in forty-eight hours.

11.6.53: The gangrenous tips of the digits were removed. Flaps were fashioned and as much of the finger preserved as possible. The pulp of the right thumb was grafted.

Physiotherapy was commenced at once. He has now returned to work.

COMMENTS

The cause of the gangrene gives rise to some conjecture.

(1) The only form of costo-cervical syndrome which would be likely to cause such extensive gangrene would be a cervical rib. This has been excluded.

(2) The distribution of the gangrene and the presence of normal pulses make an embolic cause unlikely.

(3) The distribution is wholly compatible with a profound and prolonged spasm of the digital arteries.

Two causes for this spasm seem possible in this case.

(1) *Cold.*—It was cold in March 1953, but the patient had noticed no undue sensitivity to cold before.

(2) *Trauma.*—This seems to be the most probable main precipitating factor. The patient says that when using a cold chisel and club hammer all the jarring occurs in the fingers and thumb of the hammer hand and in the fingers of the chisel hand most used for steadying the chisel—in his case the middle and little fingers. I have tried this myself and agree with his observations. Whereas this would not cause spasm of normal digital arteries, it is suggested that use of the pneumatic drill may have sensitized the vessels.

This condition is probably allied to the spasm associated with the use of vibrating tools although gangrene in such cases is reported to be very rare, but does occur in patients over 50. This man is 50.

I performed a sympathectomy as the patient's fingers were constantly cold in spite of the œdema and inflammation associated with the gangrene. The great improvement in the finger circulation which resulted and the satisfactory healing of the amputation wounds seemed to justify the operation. A modification of the Goetz approach was used in that the operation was entirely extrapleural. This tends to prevent post-operative chest complications and minimizes the risk of disturbing an old apical tuberculous lesion.

Recurrent Hyperthyroidism.—SELWYN TAYLOR, M.Ch.

Male, aged 41, referred by Dr. R. S. Bruce Pearson.

History.—1939: Hyperthyroidism of rapid onset following a road accident. Staged thyroidectomy at Leeds followed by gain in weight, but he remained somewhat hyperthyroid and suffered laryngeal spasms.

1942: Discoloured patches appeared on front of both legs (Figs. 1A and 1B). The thyroid enlarged and his eyes became prominent.

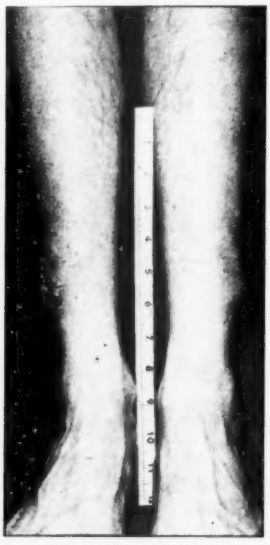


FIG. 1A.—Bilateral pre-tibial myxœdema.

FIG. 1B.—The lesion on the right leg.

1946: Signs of hyperthyroidism became more marked and he was given thiouracil which he took fairly constantly for subsequent six years.

1952: The exophthalmos became worse and he had transient blindness.

5.11.52: Given radioactive iodine therapy—26 millicuries after preparation with methyl thiouracil. This dose proved insufficient to return him to a euthyroid state.

14.1.53: Started pituitary irradiation by two opposed 6 × 8 fields to the mid-line, for three weeks, dose 3,000 r. The patient suffered no substantial disturbances as a result of this treatment but offered the opinion that the swellings in front of his shins had started to lessen.

28.4.53: The patient was again prepared with methyl thiouracil and given 23 millicuries of radioactive iodine. The estimated size of the gland was 130 grammes and his excretion rate was 32·5% in the first forty-eight hours.

27.5.53: Reported feeling very much better, but now had clumsiness of the right hand and found himself putting his hand to the right of objects. Examination revealed weakness of the right hand and some wasting of the right shoulder girdle. There was no sensory loss. The weakness of the muscle groups in the right arm appeared proportionately equal in both proximal and distal groups. The right arm "fell away" if extended and there was more tremor in it than on the left side. There was slight weakness of the flexors of the right thigh and coarse fasciculations were noticed in the right calf.

COMMENT

This patient is presented as one of recurrent hyperthyroidism treated both by surgery and radioactive iodine. He shows pretibial myxœdema, severe exophthalmos which appears to be arrested, and moderate ophthalmoplegia. He has had irradiation of the pituitary. He now shows muscle wasting on the right side which may be due to thyrotoxic myopathy. Against this is the fact that it is of unilateral distribution and noted by the patient to be distal rather than proximal. X-rays of cervical spine are normal.

POSTSCRIPT.—Patient seen on 9.12.53 and has completely recovered from his myopathy.—S. T.

Prostatic Carcinoma with Pulmonary Metastases: Spontaneous Remission.—H.-J. B. GALBRAITH, M.D., M.R.C.P. (for N. C. OSWALD, M.D., F.R.C.P.).

S. S., male, aged 56.

History.—October 1947: Fatigue and left lower chest pain began.

July 1949: Inoperable pulmonary neoplasm diagnosed following chest radiography which showed a right hilar mass, elevation of the left diaphragm and circular shadows in both lungs.

1950: Onset of cough, productive of mucoid sputum, and dyspnœa. Malaise, often necessitating bed rest, and loss of weight.

July 1950: Chest radiograph: Numerous spherical deposits in both lung fields with enlargement of the upper mediastinum (Fig. 1).

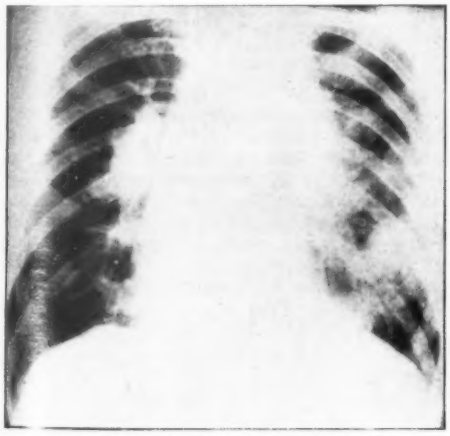


FIG. 1.—Condition in July 1950.

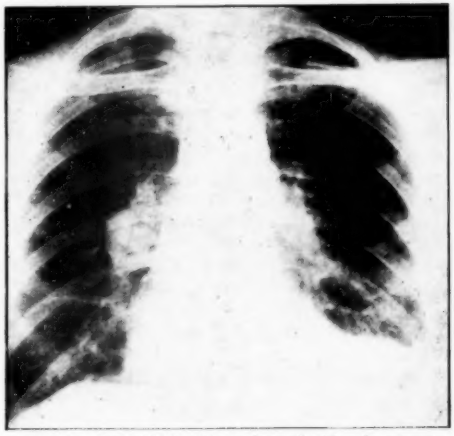


FIG. 2.—June 1951. Note the reduction in upper mediastinal and pulmonary shadows.

June 1951: Spontaneous clinical improvement lasting several months with disappearance of malaise and cough and gain in weight. Coincident radiological improvement (Fig. 2).

November 1951: Severe chest pain. Dyspnœic at rest. No urinary symptoms. Referred for investigation.

On admission.—Temperature 97°–99·4° F. Ill. Jugular venous engorgement. Signs of a large left pleural effusion. Liver palpable. Firm, irregular prostatic enlargement.

Investigations.—Pleural fluid: sterile, lymphocytic.

Chest radiograph (after aspiration of 5½ pints of fluid from left pleural cavity): Numerous secondary deposits in both lungs, recurrence of upper mediastinal enlargement (Fig. 3).

Serum acid phosphatase: 12 King-Armstrong units; alkaline phosphatase: 12 King-Armstrong units.

Radiographs of spine and pelvis: No bony metastases.

Progress.—December 1951: Treatment with stilbœstrol, 10 mg. t.d.s. begun. Thereafter there was a slow steady improvement with disappearance of cough and hepatomegaly, gain in weight and return of serum acid phosphatase to normal (1 King-Armstrong unit). Radiographs showed gradual disappearance of the pulmonary metastases during the next three months.

February 1953: Dosage of stilbœstrol reduced to 5 mg. b.d. as maximal improvement had been obtained.

October 1953: In good health, with no cough and only slight exertional dyspnœa. Takes stilbœstrol, 5 mg. b.d., which has produced no gynæcomastia or other side-effects. Chest radiograph unaltered for the past year (Fig. 4).

FIG. 3.—November 1951.

FIG. 4.—October 1953. Left diaphragm moves normally, but poorly, on respiration.

COMMENT

Although no histological proof was obtained, the clinical characteristics of the prostate, the raised serum acid phosphatase, and the dramatic, sustained, response to treatment with stilbœstrol leave little doubt that the diagnosis of carcinoma of the prostate is correct. The cause of the spontaneous remission, in which both clinical and radiological improvement occurred, is less certain. Huggins (1946) has suggested that prostatic carcinoma in its early phases may be dependent on the presence of circulating androgens for its growth. It may be that, during the severe illness which immediately preceded the spontaneous remission in this patient, the endogenous production of androgens was depressed and that thus the neoplastic process was temporarily arrested.

REFERENCE

HUGGINS, C. (1946) *J. Amer. med. Ass.*, **131**, 576.

Section of Comparative Medicine

President—Professor T. J. Bosworth, M.A., B.Sc., M.R.C.V.S.

[*October* 21, 1953]

Control of Livestock Diseases in Britain: Some Reflections on the Present Situation

PRESIDENT'S ADDRESS

By Professor T. J. Bosworth, M.A., B.Sc., M.R.C.V.S.

We live in an age when the livestock industry of this country has reached a higher state of development and is of immeasurably greater importance to our economy than it has ever been in the past. We have been warned repeatedly that we can no longer count on being able to cover all our deficiencies in food production by purchase from abroad because of the growing demand on existing supplies of a rapidly increasing world population and, further, that we could not afford to buy as much as we would like even if ample supplies were available. However that may be, it seems certain that the more food we can produce at home the greater will be our prosperity in peace and our safety in time of war. One of the important problems which faces us, therefore, is how we can best ensure that the health and productivity of farm animals are maintained at the highest possible level.

Much of the newer knowledge regarding diseases and disease-producing factors which is the basis of many advances in preventive and curative medicine has been obtained from the study of animal diseases themselves but veterinary practice, like medical practice, has benefited to a considerable extent also from original scientific discoveries of a more fundamental and general character which have been found to be applicable to its own particular problems. During our time the study of vital processes in general, including those of disease, has been advanced at a far greater rate than ever before. New sciences have been directed to this study, new fields of investigation opened up and many new technical methods, some of them quite revolutionary in nature, are being applied. On the face of it, therefore, the future would appear to be full of promise, but I personally am not satisfied with the present position regarding animal disease in this country.

Epizootic Diseases

Much of the progress made in the control of animal diseases has been related to those which are infective in nature. There is an important group, the so-called epizootic diseases, which are scheduled under the Diseases of Animals Acts. Here Great Britain enjoys an advantage over most countries by reason of her geographical position, which materially helps to prevent the introduction or reintroduction of infection from abroad. Hence cattle plague, contagious bovine pleuro-pneumonia, sheep pox, glanders and epizootic lymphangitis of horses were long ago eradicated and have never recurred. It is true that rabies was reintroduced after the First World War through a breach of import regulations but there has been no further recurrence since that outbreak was suppressed. Parasitic mange was eradicated two years ago and sheep scab has almost, if not quite, reached vanishing point. Neither of them is likely to give trouble in the future. Of those that remain foot and mouth disease, swine fever and fowl pest are viewed with real concern and anthrax is an annoyance.

Foot and mouth disease.—The great menace which this constitutes to our flocks and herds was amply exemplified by its most recent visitation from the Continent which occurred nearly two years ago. At one time it spread so fast and affected so many animals that there were misgivings as to whether it could be got under control by the policy of slaughter except at too great a cost in cattle and money. As has happened before in such circumstances the policy became the subject of vigorous criticism, much of it singularly ill-informed, though perhaps understandable in the circumstances. In view of the seriousness of the outbreak a Committee was set up "To review the policy and arrangement for dealing with foot and mouth disease in Great Britain and to advise if any changes should be made in the light of present scientific knowledge and the technique and

administrative experiences gained in recent years in this and other countries". The Committee has travelled very widely in the execution of its task and studied all sides of the question. Its report is awaited with interest and we cannot be sure what it will contain. The slaughter policy has the strong support of the veterinary profession and the farming community of this country. The grounds on which that support is based are very strong ones indeed and I shall be surprised if the Committee, after sifting all the evidence they have heard at home and abroad, does not reach the conclusion that it would be greatly to our disadvantage to abandon the slaughter policy, at any rate until a completely effective method of protection has been elaborated and then only if its use can be justified on economic grounds.

Swine fever.—As is the case with foot and mouth disease, swine fever is likely to remain a continual hazard so long as we import the infection in meat from abroad. The numerous cases which have occurred during the last few months have drawn attention to the need to encourage farmers to use crystal violet vaccine, a safe and reliable prophylactic. Normally they are loth to go to this trouble and expense unless there is immediate risk of their animals being exposed to infection. As a result nearly all pigs in the country to-day are susceptible but a scheme is now being put into effect which should encourage the use of vaccination as a routine procedure, particularly among breeding stock.

There appear to be great possibilities in the lapinized virus recently introduced as a vaccine in America and it is to be hoped that it will prove possible to adapt it for use in this country, for not only is it capable of stimulating a stronger and more durable immunity than crystal violet vaccine but it is much easier to prepare and handle. There is also the hope that extension of vaccination in countries from which we import pig meat will materially reduce the incidence of virus therein.

Fowl pest.—Here the situation seems more complicated and this is the one epizootic disease which has become more troublesome in recent years. Following the original outbreak in 1926 and the second one in 1933 it was not seen here again until 1947 when it became widespread as the result of infection introduced in carcasses from abroad and was only controlled by rigorous measures involving the prohibition of movement over wide areas and the slaughter of affected and in-contact birds. Though the imports have been controlled since 1950 the disease has continued to occur with a fluctuating incidence due partly to contact with infected swill from ships and also partly, it is to be feared, to the disease having become endemic in a few areas. The situation calls for vigorous measures aimed at the detection and elimination of affected flocks, for the disease, when not in the acute form, can be most insidious. That it may cause endless trouble if it once becomes firmly established, is evident from experience in America and other countries where resort has had to be made to vaccination which, though it produces a lasting immunity, has certain disadvantages inherent in the tendency for the vaccine strains of virus to spread to other birds and raise difficulties with regard to diagnosis and otherwise.

Before leaving the subject of epizootic diseases I would again emphasize the value of the restrictions we impose on the import of living animals into this country. We are not infrequently reminded of the protection they afford us against rabies, cases of which occur from time to time in animals during the quarantine period when they can be dealt with safely. Attention has also been drawn to this matter recently in connexion with the importation of live pigs from Sweden and the risk that they may bring with them a disease, contagious rhinitis, from which British pigs have so far been immune. As this is a very insidious complaint the pigs are being kept under close observation for a year or two to enable prompt measures to be taken in case the disease should appear. Concern has also been expressed as to the possibility of these imported pigs being affected with trichinosis and *Cysticercus cellulosæ* infection (the cause of measly pork) from both of which British pigs have long been free. Here it would be very difficult to specify any period of quarantine which could be regarded as safe and both these parasites may infect man. To illustrate the danger a well-known member of our meat inspection service has pointed out that *Cysticercus bovis* infection (measly beef) which was almost unknown in British cattle before the Second World War, is now met with daily in abattoirs due, it is believed, to the influx of European refugees during the war. Viewed in this light, import restrictions, however drastic they may appear on the surface, are not to be regarded as a mere nuisance.

Non-scheduled Diseases

I now turn to other affections of a more insidious nature, the effects of which are not so striking as those of the epizootic diseases but which are even more important from an economic point of view. Let us take, for example, those which at the outbreak of the last war were considered of outstanding importance as major diseases of dairy cattle—tuberculosis, brucellosis, mastitis and Johne's disease—and look at the position to-day.

Tuberculosis.—The first serious attempt systematically to tackle the problem of tuberculosis among our cattle was the introduction by the Ministry of Agriculture in 1935 of the attested herds scheme which aimed at building up clean herds by tuberculin testing and the elimination of reactors. A good start had been made when war broke out, particularly in areas where the incidence of the disease was low, but the scheme was then partially suspended. Since being brought back fully into operation in 1942 it has made substantial progress. The number of attested herds has risen rapidly from 17,000 in

1948 to 90,000 in 1952, the latter figure, according to the latest published records, including nearly four million head of cattle or 42·5% of the total cattle population. The scheme is on an entirely voluntary basis but it offers herd owners a number of inducements in the shape of various bonuses on milk sales, improved market value of animals, particularly of pedigree stock, and better health generally. When a substantial proportion of the herds in an area of suitable dimensions has been attested, powers are taken to declare it a so-called "free-testing" area, which means that the Ministry undertakes for a given period to test the other herds in the area with a view to their qualifying as attested herds. At the end of that time any remaining herds are compulsorily tested, reacting animals are slaughtered, and compensation is paid to the owners. When all reactors have been removed the area is declared an attested one. At the present time approximately 20% of the total cattle in Britain are included in one or other of these types of area, all of which should shortly qualify as attested areas. Many of these areas are those in which the original incidence of the disease was low but good progress is being made in other parts and, although some of the worst affected will remain to be dealt with last, there are grounds to justify the hope that the process of elimination will be completed throughout the country within a reasonable time and will, moreover, be carried through without any serious effect on the milk supply. The fear of this was at one time held to exclude the application of such an attempt to eradicate the disease in a country where its incidence was as high as here. The Danes have just announced that they have succeeded in eliminating the disease in their cattle after a campaign lasting eighteen years, and the Swedes, who started in 1937, have not much farther to go. But for the unfortunate decision to suspend our scheme during the war we might by now have been within measurable distance of the same goal. The elimination of bovine tuberculosis from cattle will lead to a great improvement in their general health and will also remove the danger of their spreading the infection to man and other animals.

Brucellosis.—The introduction of S 19 vaccine in 1944 has done much to reduce the losses due to abortion and infertility which result from the disease. This is an instance where a policy of vaccination appears to have practical and economic advantages over the alternative one of attempting to build up and maintain herds free from infection in face of all the difficulties that exist. Though the method may not provide a solution to the whole problem, the results of its use, so far, suggest that the incidence of brucella infection is being reduced and may eventually reach a point at which the institution of a programme for its complete elimination might be considered. This was the idea with which the vaccine was first introduced in America.

Infertility.—As mentioned above, the use of S 19 vaccine has removed one of the most frequent causes of impaired fertility in cattle. The study of many other aspects of the condition, which may be of genetic, nutritional, hormonal or infective origin, has yielded information of value in prophylaxis and treatment but there are many obscure problems awaiting solution in this sphere. The practice of pregnancy diagnosis has been of great service in revealing the existence of infertility and permitting early investigation of its origin in bulls and cows. In this connexion the importance of semen quality is widely recognized especially in relation to artificial insemination programmes. This practice of artificial insemination is now well established in this country. It has shown itself capable of improving the quality of our herds as well as playing an important part, subject to proper safeguards, in reducing the spread of venereal diseases.

Mastitis.—Considerable relief from the almost hopeless position in which we for so long laboured in seeking an effective means of controlling mastitis in cattle, was at last obtained when penicillin became freely available for use in veterinary practice. It is effective in the treatment of the common contagious form of the disease caused by *Streptococcus agalactiæ* and it, along with other antibiotics, has been used with a fair but by no means uniform measure of success against most of the other forms. Much has been learned of the factors which predispose the udder to infection and this has been applied in devising preventive measures.

Johne's disease.—This is proving one of our most difficult problems and we are in little better position to-day than in the past. The disease appears to have become more widely spread and there are those who now regard it as the most important disease of cattle in many areas. We have learned much in recent years about the causal organism and its habits and have come to appreciate its wide distribution among the cattle population involving as it does a high proportion of cases of latent infection to those of overt disease. We are thus only now beginning to realize the extent of the problem. The two most promising lines of control would appear to be (*a*) the rearing of calves free from infection so as to avoid the risk of contact during the most susceptible period of their lives, and (*b*) vaccination which, though it has some drawbacks, appears to convey a measure of protection in the majority of cases. Unfortunately the diagnostic tests are not of sufficient specificity to serve as a basis for an eradication scheme like that now in operation against tuberculosis because they yield cross reactions in animals infected with other acid-fast bacteria.

The Trend of Infectious Diseases

In this brief survey of some of the more important infectious diseases there have been several indications of the fact that the overall disease picture is subject to continual change. This is seen to

occur partly as a natural phenomenon, partly as a consequence of some action deliberate or otherwise on the part of mankind. Frequently the cause is hard to find. Forty-five years ago *Salmonella abortus equi* infection was a menace to the thoroughbred breeding industry of this country but it disappeared soon afterwards for no apparent reason and to the best of my knowledge has not recurred.

A similar disease in sheep due to *S. abortus ovis* which was at one time prevalent, particularly in the Eastern Counties, is now seldom encountered. An even more striking and providential example of recession of incidence occurred in the case of neurolymphomatosis of fowls which, prior to the Second World War, had gained such a hold, in the ten years or so since it was first recognized here, as seriously to threaten the prosperity of the whole poultry industry. A marked improvement followed the compulsory reduction in poultry stocks necessitated by the war and it has since been largely maintained. Again, as the incidence of brucellosis has been reduced by the use of S 19 vaccine, not only have abortions due to *Vibrio fœtus* been more frequently detected but this organism has come to be recognized as a frequent cause of venereal infection, capable of bringing about the termination of pregnancy in its early stages and thus an important cause of infertility, so-called. These are only a few of the examples which might be quoted, but they serve to emphasize the fact that the underlying causes of such phenomena demand the most careful study. Many aspects of the natural history of disease have in the past received scant attention in face of the overriding need to devise methods of prevention or treatment, specific if possible, and it is clear that ætiological, epidemiological and ecological considerations have too often been neglected. These are fit subjects of long-term research which could well be undertaken in university departments.

Among the diseases which fall into other categories I would just mention those due to vitamin and mineral deficiencies—absolute or conditioned, mineral imbalance, effects of trace elements, endocrine and other metabolic disturbances; a vast field of which only the fringe is as yet explored. These factors all have a tremendous influence on animal health and production. They present many difficult problems, some of which have long defied solution and others are constantly arising as the result of changed methods of crop and animal husbandry. New systems of management of grassland and fodder crops have subtle effects on animal nutrition and well-being. These constitute a challenge to veterinary science which has become so many-sided that it can only be met by the most comprehensive organization of effort.

Requirements of the Situation

Our general position in regard to the maintenance of animal health in the widest sense of the term, and this implies the maximum efficiency in production, calls for most careful consideration. Our losses from disease alone are enormous. The latest estimate is that issued by the Organization for European Economic Co-operation (O.E.E.C.) in a report on the control of livestock disease in European countries (1952). This was drawn up by a working party of veterinarians appointed to examine the existing position of control of the diseases of livestock in member countries. They reported that "the losses caused by livestock disease in the United Kingdom, for instance, have been conservatively estimated at about £80,000,000 per annum or about 15% of the value of the total output of livestock products". This is a situation which we cannot afford, but it can only be improved by the acquisition of more knowledge and by the fuller application of what we already possess. It demands increased expenditure on research, more trained personnel and better organization. The money should be made available from Government sources. A sum equivalent to quite a modest percentage per annum of the estimated loss would permit of considerable expansion of research activities if sufficient workers were available. At present many potential research workers are attracted to clinical practice by the better financial prospects it offers and teaching is also adversely affected thereby. It seems reasonable that the salary of one engaged in teaching and research should be equivalent to that of the clinician and eventually no doubt this principle will be conceded.

Of very special importance is the organization of research and this has so far proved inadequate to meet our current needs in connexion with animal health and disease. At present it is in the hands of the Agricultural Research Council which also advises on all that pertains to the numerous other sides of agricultural production. Lord Rothschild, the Chairman of the Council, has recently expressed the opinion that "the present organization of Agricultural Research in this country is clumsy, irritating and ripe for rejuvenation". I would go further and suggest that his Council is charged with a task which it is beyond the capacity of any single body to undertake successfully and the sooner this weakness is recognized the better. The problems of animal health in their scope and complexity as well as in their nature are just as formidable as those which confront the Medical Research Council and there is every reason why they should be entrusted to a separate body constituted on analogous lines which would study and advise on the present situation and would foster the necessary research programmes.

Proceedings of the Royal Society of Medicine Vol. 47 27

Section of Urology

President—HUGH DONOVAN, M.B., F.R.C.S., F.R.C.S.Ed.

[*October* 22, 1953]

Malignant Cachexia

PRESIDENT'S ADDRESS

By HUGH DONOVAN, M.B., F.R.C.S., F.R.C.S.Ed.

The Queen Elizabeth Hospital, Birmingham

ABSTRACT.—Well-known authorities such as Ewing and Willis have thrown doubt on the existence of a constitutional effect of malignant disease other than that due to hæmorrhage, infection, mechanical pressure, &c. On the other hand, Greenstein has taken the opposite view and maintains that a local malignant growth has a general constitutional effect.

The clinical picture of malignant cachexia is as clear cut as that, for example, of old age. Malignant cachexia is a recoverable state in certain circumstances when the primary growth is removed; clinical evidence warrants the conclusion that it is a genuine entity and that it is a generalized disease. The laboratory findings have not established that the degree of depression of any one system is the predominant cause of death. Clinically, however, the most deadly effects seem to be those produced on the cardiac and alimentary musculature. Experimental evidence would seem to have shown that there is a specific effect, chiefly on one of the cellular enzymes, catalase, predominantly in the liver but also to a lesser extent in the kidney. There is also a marked effect on the blood-forming organs. Greenstein's view that there is depression of the metabolism of the iron porphyrins naturally attracts our attention. Whether this effect is the result of some substance added to the circulation or taken from the circulation is uncertain, but an additional effect seems most probable.

Tissue culture may enable us to confirm the existence of the metabolite responsible, and perhaps to identify it. The hitherto untreatable anæmia of malignant cachexia gives us another line of investigation.

THE urologist is in a peculiarly fortunate position to study the condition of malignant cachexia, for cancer of the kidney and cancer of the testis frequently cause it in a comparatively uncomplicated form.

We have now reached a stage in the study of malignancy which is interesting and satisfying, satisfying because so much positive knowledge has been accumulated that the possibility of understanding the process is beginning to emerge. To me it seems that we have at least three major problems to solve. The first is: what chemical changes take place in the cell to make it become as we say, malignant, causing it to embark on its course of irreversible division, maintaining itself and largely ceasing to function. The second is: what is the explanation of its other new properties. Why can a neoplasm, for example, metastasize? A split skin graft will not survive unless it is autogenous, and its destruction is thought to be due to antibody formation by the recipient. A malignant growth is almost the only protein complex which can be transplanted into another host without generally evoking a manifest allergic reaction. Again, when the body is injured—for example, when the kidneys are severely bruised or ruptured—it is very likely indeed that cells are displaced into the circulation. Yet there is no very certain evidence on record of metastasis of normal tissue. My colleague, Dr. D. L. Woodhouse (1941, 1953) in the Cancer Research Department of Birmingham University, has carried out some experiments to study this problem, so far, I understand, with negative results. The third problem—which is the subject of my paper—is why does the growth kill the patient.

THE CLINICAL PICTURE

We are all only too familiar with the clinical picture of malignant cachexia, the unsmiling, wasted face, the somewhat sallow and occasionally anæmic complexion, the languid air, the flaccid dry skin, the complete lack of energy, the loss of appetite, the history of loss of weight, and not infrequently the infection of the mouth with thrush. Strange to say, typical as this picture usually is, with its many positive and also negative features, there are those who deny that it is a real entity, and who insist that the fatal illness from malignancy is due to well-known and obvious defects. A leading exponent of these views is Professor R. A. Willis (1948) who states that the condition is accounted for without postulating toxins or an extravagant nutritional demand by the tumour, and that it is the

result of such factors as starvation, hæmorrhage, ulceration, bacterial infection, destruction of functionally vital tissues e.g. bone-marrow, pain, sleeplessness and anxiety. Ewing (1940) states "our present knowledge derived from careful clinical studies, from observation at autopsy, and finally from chemical investigation, seems to warrant the conclusion that a peculiar toxin secreted by cancer cells and leading to cachexia does not exist".

That certain malignant growths at any rate, give off abnormal substances into the blood stream, is a matter of common knowledge. Four well-known examples are the increased serum acid phosphatase in cancer of the prostate, the Bence-Jones proteinuria in myelomatosis, the excretion of melanin in the urine in some melanotic growths, and disturbance of temperature in tumours, for example, of the kidney, no doubt due to some pyrogen in the circulation. These constitutional effects are, of course, not manifestations of cachexia. They are merely quoted as examples of constitutional effects produced by a localized growth.

In direct opposition to the views of Willis and Ewing, we have those of Greenstein (1947, p. 316) who, in supporting the view that a local growth has a constitutional effect, states that "the unhappily familiar cachexia of patients with advanced neoplastic disease is a clinical symptom of these effects—sometimes considerably exaggerated, sometimes masked as a result of secondary causes . . . but nevertheless fundamentally due to systemic alterations produced by the tumour on the host".

He considers that these effects may be produced either by liberation into the blood stream of material produced by the tumour, or by an abstraction by the tumour of some component in the blood stream essential for the maintenance and proper function of the distant tissues. This opinion is supported by a great deal of experimental information which I shall mention later.

It is clearly of considerable practical importance to decide which of these authorities is right. Is malignant cachexia in the absence of hæmorrhage, ulceration, or a mechanical effect, due to dissemination of the growth with bone-marrow displacement, &c.? If so, it is an indication of inoperability. If, on the other hand, this type of illness can be produced through the blood stream without dissemination of the growth, then clearly it is not an indication of inoperability. Furthermore, though this is, of course, very speculative, if there is a constitutional effect produced through the blood stream by the growth, we might venture to hope to be able to counteract it, perhaps by some medical means, and thereby to improve the quality of the patient's life and perhaps to prolong it, even though we cannot cure him. In this connexion, it is very interesting to note that some cancers do not appear to produce as grave a disturbance of health as others, a good example being cancer of the prostate.

I suppose I might say also that even if a study of the condition leads to no practical results, it is a poorly explored field, investigation of which has an interest of its own.

To help to focus attention on this matter, here are the histories of the following patients seen recently.

Case I.—F. J. W., aged 61. First seen in May 1953, with only a three weeks' history of which the first symptom was pain in the loin. This was followed by hæmaturia and, two weeks before admission, by swelling of both legs. Death took place 1.6.53 about six weeks after onset of symptoms.

The post-mortem showed the patient to have a highly anaplastic carcinoma of the kidney. There were secondary deposits in the lung but the liver was free from growth.

The following are the results of tests taken over one week:

Blood pressure (12.5.53) 130/80. Blood count: R.B.C. 4,390,000; Hb 90%. Blood urea 32 mg.%. Serum sodium 305 mg.% (133 m.eq/l); serum potassium 22 mg.% (5·65 m.eq/l); serum chloride 360 mg.% (102 m.eq/l).

Plasma CO_2 combining power 50 vol.%; plasma pH 7·40.

Liver function tests: Serum albumin 4·5 g./100 ml., serum globulin 2·5 g./100 ml., serum-free cholesterol 92 mg./100 ml., serum ester cholesterol 150 mg./100 ml., serum alkaline phosphatase 11·6 units/100 ml. (Jenner and Kay).

van den Bergh: The direct reaction is negative; the indirect reaction is negative.

Cephalin cholesterol: negative. Thymol turbidity: 0·5 unit. Thymol flocculation: Nil.

Colloidal gold: Patterson: 1; Maclagan: negative.

Urine: sterile.

ECG.—Sinus rhythm, rate 98; rather low voltage of ventricular complexes in limb leads; no other abnormality.

No pyrexia. Temperature reached 99° F. on three occasions. Patient's clinical condition was characterized by wasting and weakness. His mind was not quite clear in the last few days.

The death of this patient within six weeks of the onset of definite symptoms does not seem accountable for on the basis of the views of Willis and Ewing.

Case II.—The second patient, P. J. G., aged 68, was investigated by a medical colleague of mine because of general failure of health with loss of weight. Examination on admission to hospital showed a cachectic and anæmic man, the only other positive finding being some occult blood in the stools. He was gastroscoped and it was thought that there was an erosion to be seen on the greater curve of the stomach. A laparotomy was therefore performed by Professor F. A. R. Stammers when it was found that there was no external evidence of a lesion in the stomach and a mass was recognized retroperitoneally in the left renal area. Further investigation showed that there was, on intravenous pyelography, a filling defect on the left side. The blood urea was within normal limits. On 7.1.53 a nephrectomy was done. The kidney was the site of a tumour of uniform yellow appearance which was reported by the pathologist to be a clear-celled carcinoma of the kidney with an unusual amount of fibrous tissue in the stroma. The patient was last seen on 13.7.53 when he was reported to have gained 2 st. in weight.

Case III.—J. P., aged 65½. Admitted under Professor W. M. Arnott in September 1948 complaining of frequency and hæmaturia. On examination, he was described as tremulous, weary and miserable. In October 1948 a left lumbar nephrectomy was performed, the kidney containing a tumour 15 × 10 cm., of yellow necrotic appearance, reported to be a Grawitz tumour. Four months later, the patient was reported to be in excellent general condition. However, he died of his disease three years after the operation.

These last two case histories do suggest that removal of the primary neoplasm substantially benefited the patient, at any rate for a time. In Case I (F. J. W.), the cause of the patient's illness to begin with was quite obscure. The last patient evidently was remarkably improved after the removal of the primary tumour. I have not sought to multiply these examples; they are a commonplace experience of all clinicians.

In investigating malignant cachexia, it is first of all worth while considering each main system in the patient. Let me emphasize at once that the patient must be studied well before the terminal phase of the disease. Osler (1917) has pointed out that patients suffering from chronic illness rarely die of the disease which brings them to their death bed. On post-mortem findings alone, paradoxical as it may seem, we would find it difficult to maintain the existence of such an entity as death from old age, and indeed it might seem that old age as a significant cause of death could be largely ruled out on the basis of Professor Willis' list of explanations of death from cancer. Of a total annual death-rate of half a million, the number of deaths from senility recorded in the Registrar-General's reports for 1950 and 1951 are just over 9,000 in each year, yet that senile decay exists is beyond any question, and no one doubts its supreme importance as a contributory cause of inevitable death.

If we study the patient then, system by system, we can say that certain systems are not materially concerned, for example, the osseous system.

At first sight the clinical evidence of significant involvement of the central nervous system is not apparent. The peripheral nervous system appears indeed to be not involved. There is no paralysis and the reflexes are not abolished. The vibration sense would seem to remain. The mind may perhaps become clouded, but usually only in the last few days or hours. It is not right to say that the central nervous system is not involved at all. The picture presented is one of a general depression of its function such as might be caused by an interference with its general metabolic activity.

With regard to the general musculature, signs of weakness in malignancy have been commented upon in a recent paper by Spachman and Daniel (1953) who found that loss of vigour as a symptom was complained of in 14 of 35 patients suffering from malignant growth of the kidney. This constitutional sign was not related to anæmia. Although it was of bad prognostic significance, nevertheless, 3 of their patients survived more than two years after operation.

Loss of appetite is one of the outstanding symptoms of malignant cachexia. Appetite is said to be due to increased gastric tone together with a lowered blood sugar. There is no well-recognized evidence of interference with the sugar metabolism, and the blood sugar did not appear to be materially abnormal in the cases I have studied. Perhaps in a few, there has been a slight delay in the return of the blood sugar to the fasting level after the ingestion of glucose. There is no ready way of estimating gastric tone. The secretion of hydrochloric acid by the stomach from my observations is not abolished or depressed to a marked degree unless of course the stomach itself is the site of a growth. Attempts to improve the appetite by ordinary therapeutic measures are virtually useless. Such drugs as hydrochloric acid, pepsin and so forth, are almost valueless. On purely empirical grounds and because of its unexplained beneficial action on the appetite in tubercle, I have tried Isoniazid on 3 patients without material improvement. It would seem likely that the failure of appetite is bound up with a general failure of tone of the muscles of the alimentary canal. Certainly, there is no real similarity to anorexia nervosa or to organic disease of the pituitary.

Bound up with the failure of appetite is the loss of weight. I think we can deny the suggestion that death results from starvation. The patient is rarely sufficiently wasted at post-mortem to make this acceptable as the cause of death. In particular, his fat depots are often not emptied. In starvation, it has been shown that the basal metabolic rate is very low. In a small series of cases of malignant cachexia which I have investigated the B.M.R. has in fact been somewhat raised, in the region of − 16 to + 20%. Moreover, in certain conditions, the patient is compelled to accept into his stomach an adequate diet, as, for example, when he has a gastrostomy. The essential need of supplying to such patients a properly balanced diet of at least 2,000 calories was pointed out many years ago and is surely well recognized. Yet patients with an adequate gastrostomy presumably given a sufficient diet, do not survive malignant obstruction of the œsophagus.

Loss of weight as a symptom in renal cancer has been specially studied by Griffiths and Thackeray (1949) who found that in 16 patients complaining of loss of weight before operation, although the symptom had a bad prognostic significance, yet one was still living after six years and 5 survived more than one year after operation. I have looked into this sign and of 100 cases of renal cancer in the records of the United Birmingham Hospitals operated on more than three years ago, I have found that 26 are still alive. Of these 26 living patients 7 complained of some loss of weight before operation.

There is no evidence whatsoever that failure of renal function is a cause of death in malignant disease unless it so happens that it is associated with obstruction of both ureters. The patient may be very ill indeed with wasting and weakness, and still have a normal blood urea and no obvious sign of renal failure.

The hæmatopoietic system is almost constantly depressed, and in the absence of blood loss and sepsis, blood counts in the region of 3 million red blood corpuscles are very common. This, however, is not a fatal degree of anæmia. Life, in the absence of malignancy, can continue for months and years with such a count, and the red cell count rarely falls below some such level. It is interesting to note that in the so-called "marble-bone" disease of Albers-Schönberg, there may be encroachment on the bone-marrow space with the production of anæmia. This disease is extremely chronic. It does not seem possible to raise the blood count by any of the ordinary means at our disposal. In this respect the anæmia bears some general resemblance to that of chronic uræmia. I suspect this is a hint of some importance, to which I will refer later on.

The endocrine glands, unless as is rarely the case, directly involved, do not show well-marked evidence of gross depression of function. The blood electrolytes are not dangerously disturbed.

The patient, though weak and depressed, has none of the usually accepted clinical signs of heart failure. In the absence of a pleural effusion, he sleeps comfortably with one pillow. His heart-rate, though perhaps increased, remains regular, and if not involved by secondary growth the liver is not swollen, and frequently there is no œdema of the legs nor albuminuria. Yet death in the end is almost certainly due to arrest of the heart beat.

Discussion

The clinical picture built up in the mind, in this disorder, is of one existing in its own right, an undoubted general constitutional effect produced throughout the body by the presence of a local malignant growth. As a clinician I have no difficulty in accepting the systems of the body as delicate sounding boards or reactors to pathological processes, and I think that perhaps it is possible to suspect what may be behind these reactions. Before developing this matter a little, I would like to discuss some of the experimental evidence and some of the modern views on cellular activity. The terminology and the techniques are somewhat unfamiliar grounds for us as urologists, but it is not impossible to follow the general gist of the lines of investigation and to appreciate what is likely to result from further exploration along these lines.

In the past, the internal chemical changes in the cell seemed so minute as to be incapable of adequate study, but by the development of many exquisite techniques and by remarkable insight, we are gradually getting in a position to make important generalizations.

Sir Rudolph Peters (1953) has stated "The wider recognition of the unique importance of intracellular enzymes in catalysing specific metabolic paths is of only recent growth and the understanding of their influence on medicine a contemporary study, the pace of which is being forced by the bridges forming between enzyme biochemistry and functional studies, in the broadest sense . . . "

It is of great interest, though perhaps not germane to the matter under discussion, to realize how conservative Nature is in the use of enzyme systems. For example, as Pryde (1931) has pointed out, the elaborate complex series of chemical changes which take place when yeast splits starch to form alcohol, have a very considerable general resemblance to the chain of reactions which occur when glycogen is split during muscular activity. And again, it is of absorbing interest to observe Nature's apparently experimental efforts in the production of oxidation in living tissues by combinations of a metal (iron or manganese or copper) with pyrrol rings, combinations—experiments, if you like, to equal her extraordinary experiments in animal external formation. It has been suggested, but unfortunately I cannot find or confirm the reference, that in the living cell there are, in fact, seven or eight basic enzyme systems.

According to Greenstein (1947, p. 318), the most striking constitutional effect in animals produced by malignant tumours appears to be in the liver. In rats, for example, carrying a wide variety of subcutaneously implanted tumours, the level of activity of one of the hepatic enzymes associated with oxidation called catalase and also the level of activity of arginase may be, and indeed usually are, considerably below the normal value. Removal of the growth will lead to a return to normal of the enzymic pattern of the hepatic tissue. This effect is not produced by, for example, pregnancy. The outstanding change in malignancy is the great depression of catalase activity chiefly in the liver but also to a lesser degree in the kidney, but there is some diminution in the activity of certain other enzymes in the liver, e.g. lipase and d-amino oxidase (Greenstein, 1947, p. 361). Greenfield and Price (1953) have isolated a fraction from experimental tumours which on injection reduces the liver catalase to approximately half of the control value in twenty-four hours. Greenstein (1947, p. 202) postulates that the marked effect of a distant tumour in lowering the liver catalase and the blood hæmoglobin of the host, would appear to suggest that there is some factor which is antagonistic to the synthesis of the iron porphyrins.

Nearly all rapidly growing tumours in mice and rats produce identical systemic effects in the host animal as shown by the marked reduction of the liver catalase activity, though even in a liver which has lost about half of its catalase activity, no microscopical changes are evident. In this respect at least, the value of the more subtle chemical techniques in recognizing such changes is apparent. It may not be so fantastic to suggest that we will soon be sending pathological specimens to the cellular enzyme chemist rather than to the histo-pathologist for report.

There seems to be considerable experimental evidence to support the theory that when a malignant growth develops in the body, it may have widespread constitutional effects, and that these effects begin to be recognizable by chemical study and that they are possibly on those enzyme systems which influence cellular oxidation or the release of energy within the cell.

Such a conception as this would seem to fit in well with the clinical picture of a widespread depression of almost every system in the body, the brunt falling perhaps on the musculature so that finally a critical degree of heart failure is reached and the heart beat stops. The experimental evidence quoted by Greenstein (1947) seems overwhelming and incontrovertible that local cancer can cause a general constitutional effect, and surely clinical experience, if properly assessed, is also unequivocal on this point.

I, for the moment, am more attracted to the view that the malignant growth excretes something into the circulation which damages the body rather than that it abstracts such a substance. I have found that transfusing a patient with blood ($\frac{1}{2}$ pint at fortnightly intervals) appeared to make no difference to the steady downward path, nor has the administration of all the known vitamins in large quantities seemed to have any significant effect. Girdwood (1953) has recently pointed out that folic acid when injected into patients in 5 mg. doses is not excreted in the usual quantity in the urine in the presence of advanced malignant disease, and he seems to favour the explanation that the tumour tissue competes with the host for folic acid or its derivatives. It so happens that I had treated a patient dying from cancer of the prostate with folic acid some months ago. I had not noticed any very certain benefit in his general condition. A single case means very little, of course, and the folic acid might very possibly have benefited the neoplasm rather than the patient.

Cruickshank (1953), working in Professor J. R. Squire's Department in the University of Birmingham, making use of tissue culture as an indicator has found that serum from a patient suffering from malignant cachexia neither inhibited the growth of the epidermis when compared with a control nor did it inhibit the rate of oxygen consumption of the cultured tissue under the same conditions. These were pilot experiments and perhaps need confirmation. It is now proposed to note whether the medium bathing a tissue culture of malignant cells becomes toxic to a culture of normal cells. If so, I think we will have something tangible to work upon. The fact that a growth of skin in culture was not inhibited by serum from a cachectic patient is not necessarily significant. If we consider that the main functions of a cell are to multiply, to differentiate and grow, to secrete and perhaps merely to live, it is quite easy to accept that only some of these functions may be depressed under certain conditions. In the patient suffering from advanced malignant disease, those tissues which ordinarily continue to multiply and differentiate in the body, are not very greatly inhibited, the leucocytes continue to be formed apparently normally, and an operation wound will heal fairly well. Although perhaps secretory activity is depressed, the outstanding impression beyond a doubt is of diminution of energy production behind every process in the body. This seems to me a valid clinical observation and one which justifies us to encourage the enzyme chemist to narrow his study down to the chain of reactions which lead to energy release. The other hint would seem to be the intractable anæmia. The suggestion of Greenstein (1947, p. 202) that there is a defect in the metabolism in the iron porphyrins may serve as a link between these two pointers and I think they open up a vista of lines of enquiry which are quite promising and which are engaging our attention.

REFERENCES

CRUICKSHANK, C. N. D. (1953) Personal communication.

EWING, J. (1940) Neoplastic Disease. 4th Edition, Philadelphia and London, p. 52.

GIRDWOOD, R. H. (1953) *Brit. med. J.*, ii, 241.

GREENFIELD, R. E., and PRICE, V. E. (1953) Proceedings of the American Association for Cancer Research. Abstract Papers. 44th Annual Meeting. Vol. I, No. 1, p. 21.

GREENSTEIN, J. P. (1947) Biochemistry of Cancer. New York.

GRIFFITHS, I. H., and THACKERAY, A. C. (1949) *Brit. J. Urol.*, **21**, 128.

OSLER, W. (1917) The Principles and Practice of Medicine. New York and London.

PETERS, R. A. (1953) *Brit. med. Bull.*, **9**, 86.

RYDE, A. (1931) Recent Advances in Biochemistry. London; p. 208.

SACHMAN, R., and DANIEL, O. (1953) *Brit. med. J.*, i, 1251.

WILLIS, R. A. (1948) Pathology of Tumours. London; p. 27.

WOODHOUSE, D. L. (1941, 1953) Personal communication.

[*November* 26, 1953]

The following cases and specimens were shown:

An Unusual Pyelogram.—Mr. J. G. YATES BELL.

Polycystic Disease of the Kidneys and Liver.—Mr. JOHN PRICE for Mr. J. G. YATES BELL.

Localized Polycystic Disease of the Kidney.—Mr. JOHN SWINNEY.

Kidney with a Simple Cyst and Carcinoma.—Mr. G. C. TRESIDDER.

Disappearance of Chest Shadows after Removal of Hypernephroma.—Mr. M. T. PHEILS.

Hypernephroma with Metastases Successfully Removed from Lung and Brain.—Mr. A. R. C. HIGHAM.

Spontaneous Rupture of Hypernephroma with Retroperitoneal Hæmatoma.—Mr. HOWARD G. HANLEY.

Spontaneous Adrenal Apoplexy.—Mr. H. K. VERNON.

Two Parathyroid Tumours.—Mr. J. H. TASKER for Mr. J. C. ANDERSON.

Vesical Diverticulum with Carcinoma in Female.—Mr. H. K. VERNON.

Anomaly of Bladder.—Mr. B. H. PAGE.

Carcinoma of Ureter.—Mr. ALEX. E. ROCHE.

(1) **Reconstruction of the Complete Penis Following Amputation for Carcinoma** (by Mr. Geoffrey Parker), **Using the Gillies Double Tube Pedicle Technique.** (2) **Reconstruction of the Penis after Ectopia Vesicæ with Prolongation of Ejaculatory Ducts to Glans (after Transplant of Ureters into the Colon in Infancy by Sir Lancelot Barrington-Ward).**—Mr. PATRICK CLARKSON.

Section of Anæsthetics

President—Professor R. R. MACINTOSH, M.A., D.M., F.R.C.S.Ed., F.F.A. R.C.S., D.A.

[*November* 6, 1953]

An Anæsthetist Abroad [*Abridged*]

PRESIDENT'S ADDRESS

By Professor R. R. MACINTOSH, M.A., D.M., F.R.C.S.Ed., F.F.A. R.C.S., D.A.

I HAVE been lucky enough to visit professionally many different parts of the world and as many of my audience will be going abroad on professional business, it occurred to me that it would be helpful if I mentioned a few of the difficulties likely to be encountered.

My first two trips abroad were as an onlooker only. In 1935 whilst still practising in London I went to the U.S.A. mainly to see the experts at work on cyclopropane, but my outstanding impression of that trip is not of the merits of this drug, but of the help it gave me in clarifying my views on the subject of choice of anæsthetic. In England at that time there was much discussion on the choice of anæsthetic for a particular patient or operation—and to me the subject was made more confused by occasional pronouncements of distinguished physicians.

I have heard it stated that ether should not be given to a patient with any chest lesion, nor ethyl chloride to anyone with a swelling of the neck: though "a whiff of gas" might be just the thing for a chronic bronchitic with a failing heart, it was dangerous for anæmic patients. I have heard it suggested that nitrous oxide was unsuitable for patients with red hair: another step farther and someone would have explained away a fatality by claiming that Evipan should never be administered on Tuesdays. The grounds for these objections were seldom more substantial than "Blank says so"—Blank being one of the known anæsthetists or physicians of the day.

In America, however, the anæsthetic procedure at any one surgical centre seemed to be standard for all patients and operations, though this procedure might be quite different from that of another surgical centre. Thus at one hospital open ether was given to all patients, at another only nitrous oxide was used, at others only cyclopropane or spinal or local analgesia. As far as I could see the end-results varied little, and I appreciated for the first time that the good and bad effects of an anæsthetic depended little on the choice of a particular agent, but much on the skill and experience of the anæsthetist with that drug.

I was surprised at Toledo to see nitrous oxide used for everything, and I was astounded at the admirable operating conditions for abdominal surgery afforded by so-called "secondary saturation" with this agent. In New York City I saw Koster operating under nothing but spinal analgesia, even for radical mastectomy and thyroidectomy. I have practised but do not advocate these procedures, but I am prepared to defend the view that if in 1935 a patient had to have his gall-bladder out with Clement or McCarthy anæsthetizing, he would have fared better with nitrous oxide than anything else. I asked Clement whether he used the then recently introduced cyclopropane and he replied "Yes, but if I need real relaxation I go back to nitrous oxide". And if at that time I was going to have my thyroid out at Koster's hands I trust I would have been given a spinal—the anæsthetic with which his team obtained their best results. For it is impossible to believe that these world-famous exponents of what might be regarded as unorthodox techniques could have stood up to daily visits from critical anæsthetists and surgeons from all over the world if they were not having results which bore comparison with any.

When I visited Koster's clinic in 1935 his anæsthetist gave 150 mg. procaine crystals dissolved in 3·5 c.c. of cerebrospinal fluid for operations below the diaphragm, and for operations above—including on the head and neck—300 mg. dissolved in 7 c.c. of cerebrospinal fluid. He had given up recording blood pressures for the simple reason that they were often unrecordable. It certainly did not need a sphygmomanometer to call attention to the profound fall in some of the cases I saw. On one occasion an onlooker could not feel the radial pulse but Koster reassured him by saying that the heart beat could readily be felt through the diaphragm. He no longer used vasopressors, but essential parts of his technique were that the patient was kept in a slight Trendelenburg position, and given additional oxygen throughout. Operating conditions were excellent and I was impressed by the well-being of the patients a few hours afterwards. Koster encouraged his visitors to walk round the wards and interrogate nursing staff and patients.

I have seldom had occasion to use heroic doses of a spinal anæsthetic deliberately to produce such widespread analgesia, but even when I give ordinary doses for abdominal surgery an appreciable fall in blood pressure is more the rule than the exception. Since my visit to Koster I have not given vasopressors to counter the fall. The criticism which this omission aroused only a few years ago seems strange in these days when hexamethonium is in such widespread use.

In the spring of 1937 shortly after my appointment to Oxford I went to America again, and like every other visitor from this country received nothing but kindness and help. At many centres the work was excellent but I must add that I have never been able to see eye to eye with those of my American colleagues who invoke "Science" to account for something capable of a much more straightforward explanation. I will give only one example: I attended a Congress of Anæsthetists immediately after which the Board Examination was held—the equivalent of our F.F.A. On the evening before the examination, one of the candidates gave us the following details: At the end of an operation he pulled out the endotracheal tube and left the patient unsupervised lying flat on his back on the operating table. He washed his hands, smoked a cigarette, and when he came back the patient was dead. On the facts presented the probable cause of death appeared to be clear. As the post-mortem examination was negative this was presented as a clear-cut case of death from vagal reflexes set up during extubation: moreover, this view was held to be quite reasonable, an article by Donald Brace (1940) being quoted to support it. I had to enter a minority protest confessing that I did not know much about vagal reflexes, but whatever their nature I felt confident they would not have been fatal if somebody had been present to hold forward the jaw of the unconscious patient.

In 1949 I gave a talk to the Swiss Congress of Surgeons and at one stage I appealed to their baser qualities by saying that the surgeon who enjoys the support of a skilled anæsthetist sleeps better, lives longer, and does better surgery. And then I thought I would bring tears to their eyes by outlining the hard life of the British Anæsthetist for the two or three years during which he is under training. When the lecture was over my spirits slumped somewhat when a well-known Professor of Surgery told me that my talk had so impressed him that he would like to send one of his surgical assistants to Oxford "for two or three weeks to learn all about anæsthetics". On the other hand, one young man in the audience, who had already served three years' apprenticeship in a University Department of Gynæcology, threw in his hand, came to England for training until he was passed as proficient, acquired the D.A. in two parts, and already has a very flourishing practice as a specialist anæsthetist in his homeland.

Spanish Civil War

My next trip abroad was an unexpected one during the early autumn of the same year, 1937. The Spanish Civil War had then been in progress for some months and owing to the shortage of certain specialists many of the wounded were not getting the attention they needed. A friend of mine, Eastman Sheehan, an American plastic surgeon, had accepted an invitation from the Franco side to deal with some of the hideous deformities resulting from face wounds and burns. After he arrived in Spain he realized that anæsthetists and endotracheal anæsthesia did not exist in that country. Only nuns were available equipped with Ombrédanne inhalers, so that his value was reduced practically to nothing. Sheehan explained the position to the authorities, and after the exchange of a few cables I was on my way to San Sebastian armed with laryngoscope and some Magill tubes.

The only shortage to which Sheehan had referred in his cables were endotracheal tubes and someone capable of passing them. I remedied these deficiencies, but on arrival I found that Ombrédanne's inhaler was the only apparatus available. There was no cylinder of oxygen or of anything else. The only drugs they had were Evipan, chloroform, ether and ethyl chloride. There was no atropine or cocaine, and no suction. Profuse salivation was accepted as an inescapable feature of anæsthesia. I think it a healthy exercise to reflect for a moment or two on how one would tackle the situation in these circumstances. I made a Flagg's can (Macintosh and Pratt, 1939) out of a Lyle's golden syrup tin and connected it almost directly to the endotracheal tube. I noted in my diary that what I missed most was a *vis a tergo*—a current of fresh gases to convey the ether vapour to the patient. I used a wide-bore endotracheal tube and cut down dead space as much as possible, but a flow of fresh gases does help to overcome any resistance to the circuit and to blow away any accumulated CO_2.

We operated principally in hospitals at Vittorio and Saragossa. Let me quote from my diary about one case:

> "Man wounded twelve hours before. The bullet had entered through the cheek leaving a perfectly clean round wound, but the front teeth were knocked out, the upper lip and nose were reduced to pulp. There was no preparation at all. The man was not even shaved. He was not shocked and I gave him Evipan, followed by ether in an Ombrédanne's inhaler. No mouth gags available. I had to introduce my tube by direct vision and the mouth was full of blood and mucus. No cocaine available. How one misses one's usual tools, but at the same time it is extraordinary with what little one can get on."

Experiences such as this have, I am sure, influenced my approach to the question of apparatus. My advice to the young anæsthetist is to learn how to manage with simple things, and how to give open ether. The time will come, when cylinders will be found to be empty, or the apparatus has broken down, or variety of drugs is absent. When everything else fails you may still find a bottle of ether by your side: and any anæsthetist worth the name should know how to give it. Once you can do this by all means pass on to something else. I expect to say something more about apparatus later.

On this trip I had my first experience of being perplexed by changes in the patient's condition during operation, which turned out to be due to an over-zealous assistant trying to help matters, without reference to surgeon or anæsthetist. There was a large oozing surface and Sheehan's assistant, to be

helpful, had been swabbing this liberally with adrenaline. The patient recovered, but not before giving me some anxious moments both before and after I found out the reason for his alarming symptoms.

I had a similar experience during an œsophagectomy in South America. A blood-pressure chart was being kept throughout the lengthy operation and it showed bewildering rises and falls. It was only when I discovered my assistant surreptitiously injecting something that I found the cause. His motives were entirely good: he was only trying to help the patient. His teaching made him unable to accept my statement that a fall in blood pressure did not have to be countered at once by an injection of one of the many "heart tonics" in which the operating theatres abounded.

Curiously enough my first trip abroad after the war was again to Spain as a guest of their Government. After my previous experience I took with me everything I was likely to need, including an Oxford vaporizer. I also had with me some curare, not to teach them how to use it, but to demonstrate its possibilities.

My first operation caused me embarrassment. It was in Madrid, on a child of 7 for cerebellar tumour. Since they had no one to give endotracheal anæsthesia it was their custom to operate on these cases under local analgesia, with the patient lightly asleep from Avertin *per rectum*. I had previously ascertained that atropine was available and asked that this should be given before operation. I induced anæsthesia with ethyl chloride and ether from an Oxford vaporizer, and only after some minutes, when the child became bubbly, did I find out that the atropine had been omitted. What should I do next? This operation had been staged primarily to show the possibilities of endotracheal anæsthesia in cerebral surgery. Many of those present had taken time off to be present. Rightly or wrongly I decided to go on: and I passed an endotracheal tube under direct vision. In those days that simple and useful little bit of apparatus, Cobb's connexion, had not been thought of, so when suction was needed the endotracheal tube had to be disconnected from the metal connexion. With an uneasy mind I allowed the operation to be started, and mucus re-collected quickly. Suction was far from easy, so I did what I should have done before—I pulled the endotracheal tube out. The patient was face down, so the tongue fell forwards, and the airway remained clear throughout the lengthy operation. The mask was held under the face, but applied to it, and the anæsthetic mixture was delivered by the pumping action of the hand bellows of the vaporizer. The mucus drained freely into the facepiece which had to be emptied from time to time. Apart from the complication I have mentioned the operation was uneventful, and the child was awake on the table.

In April of this year I was in the Far East with a World Health Organization team, doing mainly thoracic surgery. There was a child of 3 for lobectomy for bronchiectasis, and fortunately it was put second on the list, and not first. I ordered only 1/100 grain of atropine as premedication, and as the weather was warm asked that this should be given a quarter of an hour before the expected time of operation. The first case was unexpectedly prolonged, and when the child was sent for the message came back that she was unconscious and cyanosed. She had been given ¼ grain morphine instead of atropine. She recovered, and the lobectomy was carried out successfully forty-eight hours afterwards. If this case had been first on the list, the faulty premedication, given only a quarter of an hour beforehand, would not have been evident. The child would probably have died during the operation, or immediately afterwards, for no obvious reason.

During my 1946 trip to Spain I derived a certain meretricious pleasure from two events. The first was giving endotracheal anæsthesia for a hare-lip operation when previously the surgeon had regarded intraoral insufflation as a luxury: and the second was demonstrating curare in a country where it was unknown.

The impact of curare in Spain was much more dramatic than in England. For one thing English surgeons were already used to relaxation. In the middle of the war Dr. W. W. Mushin and I obtained curare powder in 100 mg. phials from Burroughs Wellcome, and very cautiously injected 2–3 mg. into patients already well relaxed with ether. With the confidence gained of experience we gradually increased the dose of curare and economized on the ether. The surgeons did not notice the change except for increased hæmorrhage due to impurities in the powder. By 1945 we were giving curare in present-day doses, supplemented by gas and oxygen, or 3–4% ether to keep the patient unconscious, and controlled respiration was routine.

The first patient to whom curare was given in Spain was a man with a large abdominal tumour, which turned out to be a multiple hydatid cyst. I quote from my notes: "I gave him Pentothal, light ether, and 15 mg. curare, the relaxation from which brought forth laughter and surprise. No oxygen available, but insufflation of the lungs with air from the bellows of the vaporizer is quite satisfactory."

On the next day 60–70 onlookers were present in the theatre. The operation was a gastrectomy. I had previously explained to the new and, I think, doubting surgeon that I would keep the patient light until he reached the peritoneum, when with one mid-line incision he was down to this at once. Chaos supervened, but luckily the syringe was already charged with 20 mg. of curare and this injected into the drip relieved the situation within a few seconds, and brought forth gasps of surprise. Here again controlled respiration was carried out with air only.

Apparatus

Foreign surgeons often refer approvingly to British anæsthesia, but I hope it is not immodest to suggest that they attribute too much of the credit for this to the chromium-plated complex apparatus they have seen in use. I personally regret the development of British anæsthetic apparatus along battleship lines. Certainly satisfactory anæsthesia can be provided with something much more simple.

There is a certain necessary minimum of apparatus, however. The only trouble is that we may not be agreed on what the minimum should be. I shall not attempt to define what is essential, but I shall mention some of the things which can be dispensed with, and some which I have found useful.

Abroad one must be prepared to anæsthetize for any operation, and I have found that I can take with me comfortably by air everything I want. Nitrous oxide, cyclopropane and closed circuit anæsthesia are not necessary in any circumstances. I feel I will lose sympathy with many of you by making a statement like that—but notice I am speaking of anæsthesia abroad and I used the word "necessary". My experiences in the R.A.F. during the war, and abroad since, convince me that we are not conferring a benefit on the inhabitants of a remote country by making good anæsthesia there depend on the importation of cylinders of gases from a distance.

With a small portable vaporizer, a hand bellows, and a needle in the vein I have been able to anæsthetize for any operation with which I have been confronted: and I cannot think of one for which it would not be adequate—but with the addition of a cylinder of oxygen for thoracic surgery.

The small hand-bellows (Macintosh, 1953) has been a boon. There is a widespread belief that curare should not be given and controlled respiration practised unless a cylinder of oxygen is to hand. This is confused thinking. The cylinder is wanted to inflate a reservoir bag, so that when the bag is squeezed the contents are transferred to the patient's lungs. For this purpose a cylinder of compressed air is just as effective. The concertina bellows allows one to dispense with both cylinder and reservoir bag since it can be used to pump fresh air into the patient's lungs indefinitely.

If respiration is to be controlled for abdominal surgery I think there is something to be said for using air instead of oxygen. Deficient ventilation is then made apparent by the poor colour of the patient—whereas it may easily be concealed by an oxygen-rich mixture. If a patient for, say, a gastrectomy is a good colour before operation when breathing atmospheric air, why should he not remain so during the operation under curare if he is adequately inflated with air?

During intrathoracic surgery different conditions obtain. Oxygenation is already deficient because of disease, and this is made worse because a considerable part of the lung is deliberately kept deflated to allow the surgeon to do his job properly. Additional oxygen here is essential.

It is only natural that your hosts abroad should confront you with anæsthetic problems which they have found it difficult to solve. The biggest demands on my time have been made by surgeons operating in the thorax and abdomen, then come plastic, neuro- and dental surgery, and only a little E.N.T. and eye work.

Thoracic Surgery

Thoracic surgery tends to be concentrated at certain centres in this country so that many a Consultant has never anæsthetized for a major thoracic operation: and because of his lack of practical experience he may think the task beyond his capabilities. Here I would like to reassure him. I agree there is less margin for error, but it is no more difficult to anæsthetize for a blue baby or a mitral stenosis or a pneumonectomy than it is for a gastrectomy or a laryngectomy or a cerebral tumour. What more can the anæsthetist do than put the patient lightly to sleep, intubate him and keep him well ventilated—and this is what he does for many operations outside the chest.

I am not decrying the work of anæsthetists who work only at thoracic units. They are doing grand work and achieve refinement denied to others, but I hold that a little more than a knowledge of general principles is necessary to ensure satisfactory results. I have never anæsthetized for a blue baby in this country, but I have in Brazil, Germany, India and Indonesia. I have never anæsthetized for mitral stenosis, pericardectomy, or coarctation of the aorta in this country, but in Bombay, during March of this year, I anæsthetized for two visiting thoracic surgeons for 20 heart operations.

Mitchell's Needle

Formerly the anæsthetist needed a tube in the trachea before he felt he had control of the situation. In these modern days of light anæsthesia and relaxants he demands an ever open vein. In some countries an intravenous drip is set up almost as a routine, but this for a variety of reasons is not always reliable. I like to be sure that an intravenous injection can be made at a moment's notice and I pay tribute to the very valuable needle introduced by my colleague, Dr. J. V. Mitchell.

With a Mitchell needle (1952) in position and a hand bellows the experienced anæsthetist can cope with a large number of anæsthetic situations, and if he adds to this equipment an endotracheal tube and a vaporizer for ether or trichlorethylene I think he can cope with anything.

REFERENCES

Macintosh, R. R. (1953) *Brit. med. J.*, ii, 202.
——, and Pratt, F. B. (1939) *Brit. med. J.*, ii, 1077.
Mitchell, J. V. (1952) *Anæsthesia*, **7**, 259.
Reid, L. C., and Brace, D. E. (1940) *Surg. Gynec. Obstet.*, **70**, 157.

Proceedings of the Royal Society of Medicine

Vol. 47
37

Section of Odontology

President—ARTHUR BULLEID, F.D.S., L.R.C.P., M.R.C.S.

[*October* 26, 1953]

The Microbe Hunters

PRESIDENT'S ADDRESS

By ARTHUR BULLEID, F.D.S., L.R.C.P., M.R.C.S.

THE history of the discovery of the "germ" world, the genius and painstaking ability of the early pioneers, the dangers they underwent, the difficulties they overcame, the disappointments they encountered, and the triumphs they achieved, make up a story of almost unbelievable interest.

The path of most pioneers is a hard and thorny one and the path of these early bacteriologists was one of difficulty and constant danger. Every obstacle was placed in their way by colleagues who had neither the sense nor the intellect to see that a new world was being opened up by these despised workers in the realm of the unseen. They were derided and scorned for holding their opinions but they kept on and finally unfolded a world of previously unseen fantastic microscopic creatures whose existence had never before been dreamed of. Perhaps the only thing in their favour was the fact that there were no Home Office regulations with regard to animal experimentation.

To-day it is quite reputable to be a man with a scientific outlook but go back a few hundred years to a time when Servetus was burned to death for daring to cut up and examine the body of a dead man and when Galileo was imprisoned for life for daring to prove that the earth moved round the sun.

The history of bacteriology is indissolubly linked with the discovery of the microscope and it is interesting to record that the compound microscope was invented before the single instrument. The credit must probably be given to the brothers Janssens possibly as early as 1590. The principal objects studied by this instrument were small animals and to this early period belongs the discovery of the "itch acarus".

Almost since the dawn of time there have been references to contagious diseases but it was Fracastorius, who was born in 1478, who first put what knowledge there was at the time on a surer foundation. He drew attention to the fact that all contagions do not behave alike, that some attack one organ and others a different organ. He stated that contagion presented three different types, viz. contagion by contact alone; contagion by fomites; and contagion at a distance. After his death his work was soon forgotten only to be rediscovered in the eighteenth and nineteenth centuries. How often in the course of history have men of great intellect postulated certain theories, how quickly they were forgotten only to be rediscovered in later years and proved correct.

It is said that the German Kircher, born in 1602, was the first man to suggest the possibility of a world of microscopic creatures though as far as I know he never discovered any. The real discoverer of an invisible world of living microscopic creatures was Antony van Leeuwenhoek born at Delft in Holland in 1632. Destined, it is said by some, to be a draper, he yet became the first and perhaps the most completely accurate of all microbe hunters. He realized that in order to study the denizens of the unseen world he must be able to enlarge them so that they could become visible to the naked eye. In his painstaking way he ground biconvex lenses to less than one-eighth inch across and mounted them in tubes of copper, silver, and gold, to construct his "single" microscopes. He probably obtained magnifications of 200–300 diameters by this means. His extraordinarily accurate descriptions of the shape and internal structure of his "little animals" suggests that in some way he must have used some form of "dark ground" illumination. He described not only bacteria but also protozoa; he carried out the first recorded work on the physiology of the bacteria, such as the effect of heat, acids, and tobacco, and he was also the first man to prepare nutrient media for his "little animals", such as infusions of pepper. The foundation of that process known as pasteurization was probably laid down by him.

Leeuwenhoek's observations on the "materia alba" from around his teeth were most accurate and illuminating so he deserves the title of first "dental bacteriologist". He did not believe in the doctrine of "spontaneous generation" though the credit of disproving this theory is ascribed to Redi and Spallanzani. In spite of Leeuwenhoek's wonderful powers of observation I doubt if it ever occurred to him that his "little animals" could be the agents of disease in man. On his death in 1723 it might have been thought that the further study of the "little animals" would come to an end but time always brings forth the man and in 1729 Spallanzani was born in Italy and became our second great microbe hunter. Paul de Kruif states that Spallanzani was not so interested in what things looked like but rather he wanted to know how they worked. He did not believe in Needham's theory of a "vegetative force"—that life could arise spontaneously from dead material. He insisted that all living things must have parents and by his numerous experiments he proved

conclusively that Needham was wrong and that even Leeuwenhoek's "little animals" must have forebears. He also proved that they could live without air and that multiplication was by fission.

Between 1713 and 1799, the date of Spallanzani's death, a number of men appeared on the scene, all with an inquisitiveness as to a possible connexion between germs and disease. Fauchard, born in 1678, gave the *coup de grâce* to the worm theory of dental caries, about which I shall speak later. Bassi, born in 1773, demonstrated the parasitic nature of the muscardine disease of silkworms and may be regarded as the founder of the doctrine of pathogenic microbes. Cagniard-Latour, born in 1777, described the budding of the yeast cell and stated that it was probably vegetable in origin. Bretonneau, born in 1771, differentiated and named diphtheria and gave the first accurate account of the pathology and specificity of enteric fever. Schwann, born in 1810, was one of the founders of the cell doctrine and proved that the vital activity of the yeast plant was the cause of alcoholic fermentation, and though this view was ridiculed by von Liebig, it was completely confirmed by Pasteur some twenty years later. Amongst all these past investigators there does not appear the name of an Englishman until the birth of Tyndall in 1820. He became interested in the study of atmospheric germs and he anticipated Pasteur in calling attention to the struggle for existence between the various forms of life. He noticed the antibiotic properties of the penicillium mould in particular.

In an extract (No. 2) on "Essays on the Floating Matter of the Air" which was published in the *Philosophical Transactions* in January 1876 he showed clearly the antibiotic properties of the penicillium mould on bacteria and he recognized three different strains of the mould distinguished by their cultural characteristics. As is also well known he was the discoverer of the process termed "fractional distillation".

The second and greatest English investigator was Lister. He was born in 1827, five years after the birth of Pasteur. He revolutionized surgery by his antiseptic treatment of wounds and only abandoned the carbolic spray after Tyndall's experiments on the floating matter in the air in relation to putrefactive infection had appeared in 1881, when it was definitely established that the suppuration of wounds was caused by germs on the skin of the patient and the hands and clothes of the operator.

Not only was Lister a great surgeon but what is not so commonly known is that he was a great bacteriologist. He was the first man to obtain, by means of an ingenious syringe technique, a pure culture of a bacterium—the *Bacterium lactis*—in his investigations into the curdling of milk. He was also a pioneer in immunology; he decided that blood must possess some peculiar property of destroying germs and he demonstrated a bactericidal agent in the blood stream which a few years previously had been postulated by Lewis and Cunningham and later by Fodor in 1866. Lister also noted the changes which took place in the vascularization of blood clot and the living new elements he saw were later proved to be the phagocytes described afterwards by Metchnikoff. Lister was a great bacteriologist because he applied his laboratory findings to his clinical work, and there would seem no doubt that he was the only man of his generation to rank with Koch and Pasteur.

Pasteur, born in 1822, was one of the greatest microbe hunters of all time, enriching every department of bacteriology. His researches proved the germ theory of fermentation, and also saved the silkworm industry of France. He set himself the task of proving where microbes came from. They could not arise from dead material, they must have parents. He proved that microbes do cause disease not only in the lower animals but in man. He concentrated on the problem of the prevention of infectious diseases by inoculation and on the processes involved in the recovery from disease which led to the creation of the science of immunology. His experiments on chicken cholera, anthrax, hydrophobia, and many other diseases are epochs in this bacteriological story. As Paul de Kruif (1927) says "Pasteur was a human, passionately imperfect microbe hunter and saver of lives" and how true is this description of the man.

Lister and Pasteur were essentially early exponents of preventive medicine—Lister seeking to attack the germs that caused the suppuration of wounds and Pasteur trying to immunize the host against the risk of infection by bacteria in a virulent form by the use of artificially attenuated cultures.

The third great microbe hunter was Koch, born in 1843. His discoveries almost staggered the world. He set out to prove the germ theory of disease and he and his disciples concentrated on the study of pathogenic bacteria, and most authorities would date the commencement of modern bacteriology from Koch's work between 1880 and 1890. In 1876 he published his researches on anthrax which he proved was an infectious disease caused by a specific micro-organism and that the disease could be reproduced at will by injection into susceptible animals. In the course of his researches he discovered and described "spore" formation in the anthrax bacillus. His discovery of the tubercle bacillus and the vibrio of cholera and a host of other diseases was epoch making. He proved that one specific type of germ caused a specific type of disease. His failure to cure tuberculosis by tuberculin must not, I think, in the light of modern knowledge be held against him. He was a great and accurate technician; he first described the "hanging-drop" preparation; the first to obtain pure cultures on solid medium; the first to stain microbes with dyes. Most authorities would describe Koch as the greatest pure bacteriologist of all time and few would deny him the title of "founder of modern bacteriology".

Though space and time prevent the inclusion of all the great investigators in the bacteriological world yet mention must be made of Roux, von Behring, and Loeffler. Loeffler was born in 1852 and

worked in Koch's laboratory and to him must be given the honour of discovering the causal organism of diphtheria. He first suggested the possibility of exotoxin production by the organism though the actual proof of his contention was due to Roux, working in Koch's laboratory. Loeffler recognized the filter-passing character of the virus of foot and mouth disease though after years of work he was unable to isolate it. Roux was born in 1853 and after Pasteur was probably the greatest French bacteriologist. He proved the exotoxin production from the diphtheria bacillus and in conjunction with Metchnikoff was the first man to transmit syphilis to monkeys.

Von Behring, born in 1854, was the discoverer of antitoxin and the principles of serotherapy. By the work of these three men thousands of lives were saved from a disease which previously had taken an almost 100% toll of lives. This list of pioneer microbe hunters would be more incomplete than it should be if it did not include the name of Metchnikoff, that excitable, and possibly half-mad Russian genius. Born in 1845 he was the founder of the phagocytic theory of immunity. Pasteur took him under his wing and gave him every facility for proving his contention that his phagocytes ate up the invading microbes. With Roux he transmitted syphilis to monkeys and proved that for a short period syphilis was a "local" disease and that its dissemination into the blood stream could be prevented by the use of calomel ointment.

In 1893 the brilliant researches of Theobald Smith, the first and greatest of American bacteriologists, proved that ticks carried the virus of Texas fever in cattle, a new and fantastic way by which a disease could be carried—by an insect. Destroy the ticks by dipping all cattle and Texas fever would disappear, and so it was. This was another step forward in the elucidation of the cause of disease.

An old doctor, termed cranky by his colleagues, shouted out that yellow fever was carried by a mosquito and the dangerous experiments of Walter Reed and his team proved once and for all that this was a true surmise. The heroism of this band of investigators was almost unbelievable and the risks they ran in the cause of humanity were quite terrifying. Once again complete success was the fruit of their sacrifices. It is the same story with the malaria-bearing mosquito which Ross discovered as Patrick Manson had told him. It is a history of painstaking endeavour finally crowned by complete success.

The last of these microbe hunters of the past whom I shall mention is Ehrlich, the originator of the side-chain theory of immunity. Born in 1854 he worked at one time in Koch's laboratory. His experiments with dyes were finally consummated by the discovery of 606, and he can rightly be named the first chemotherapist.

So this very brief but intensely fascinating history of bacteriology has been unfolded. First the discovery of a world of living microscopic beings; then the proof of their connexion with disease in the lower animals and man; then the story of the resistance to infection and the treatment of infectious diseases by vaccination, drugs, and chemotherapy and now the knowledge of and treatment by antibiotics. A wonderful ladder of which the last rung has not yet been reached.

Where and when in this wonderful history does the bacteriology of dental disease find a place? Dental decay was noted from the very earliest times and probably the first mention of the disease, as Mrs. Lindsay pointed out in a paper in the *British Dental Journal* in November 1929, was a translation of the Babylonian Tablet 55547 in the British Museum. In the Vedic hymn No. 23 appear these lines "we will destroy the worms that creep around the eyes, the worms that crawl about the nose, and get between the teeth". There is no doubt that the so-called worms were thought in the very early days to be the cause of toothache and many authorities describe worms coming out of the teeth.

Dr. Cumston has stated that the earliest phase of medicine was a theological one and diseases caused by the wrath of the gods could only be cured by prayers. Familiar with putrefaction and the manner in which myriads of crawling worms devoured the dead tissue, they naturally concluded that teeth which were decayed and fell to pieces had been attacked by worms. Treatment of toothache was by fumigations made from the seeds of hyoscyamus followed by rinsing the mouth with hot water whereby the worms were expelled.

That worms were not the cause of tooth decay was proved by Fauchard in 1728 and he is credited with having given the *coup de grâce* to the worm theory, though one suspects that he himself was not quite convinced that there may not have been some cases in which worms were the agents of disease, though not the sole cause.

Dr. Strickland reported a case of dental myiasis in 1928 in a coolie woman in which numerous maggots were found in a carious molar, all the other teeth being sound. He could give no explanation as to the manner in which the parasite had established itself in the mouth. Capt. Grennan also described a case in 1946 in which maggots appeared in gum lesions in a West African native. Larvæ of the maggots were allowed to complete their development and turned out to be *Chrysomyia bezziana*. There thus may well have been an occasional case to keep alive the worm theory as a cause of disease, including dental disease, which was believed by many people living in the dim and forgotten past.

It can safely be said that the work of Pasteur stimulated research not only in general but dental bacteriology. Amongst the first dentists to interest themselves in the bacteriology of the oral cavity was Miller born in 1853. Working in Koch's laboratory he isolated many different types of mouth

organisms and discovered the fact that bacteria in the dentinal tubes of carious dentine when cultured in the presence of sugar or starch produced lactic acid which dissolved the calcium of the tooth. Miller's contributions from 1882–1884 were published in his book "Micro-organisms of the Human Mouth". He is generally credited as being the author of the chemico-parasitic theory of caries though I think the honour should really be given to Arthur Underwood and Milles who in 1881 described a "septic" theory of caries in which the acids which destroyed the enamel of the tooth were the result of bacterial activity. Underwood thus preceded Miller by about three years. He also drew attention to the fact that decalcification was not necessarily caries.

If we go back nearly a hundred years before Miller to 1760 we meet a most remarkable man, John Greenwood, the Father of American dentistry. He attributed decay of the teeth to external agencies, either to acid formation, a chemical concept, or to bacteria.

G. V. Black was also a student of bacteriology in America and took a most active interest in the germ theory of disease. He stated quite definitely that the acids formed in the carious process were the products of fermentation of food debris by bacteria.

In 1878 Leber and Rottenstein published a book on the nature of dental caries which makes fascinating reading for the student of bacteriology. Their description of the *Leptothrix buccalis* is of great interest though the authors could not agree as to the exact role played by the organism in relation to caries. Quoting Hallier the authors state that the leptothrix was only a form of development of the fungus *Penicillium glaucum*, a most interesting observation when one considers the date of the communication.

In 1903 Goadby published "The Mycology of the Mouth", the first textbook written by an English dental surgeon primarily for dental students, and describing the bacteriology of the dental diseases as known at that time. Goadby was amongst the first to describe the *Lactobacillus acidophilus* though he labelled it the *Bacillus necrodentalis*. He was the first man in this country to offer a classification of the bacteria concerned in dental caries. His division of the organisms isolated into acid and proteolytic groups was a great advance. His book "The Diseases of the Gums and Oral Mucous Membrane" (1922) was one of the earliest contributions on the bacteriology of these dental tissues.

The discovery of penicillin by Sir Alexander Fleming and its development by Florey and his co-workers brought the study of the antibiotics into the forefront of bacteriological research and opened up a vista of success in the fight against disease of which even Pasteur could not have dreamed.

It would seem obvious that in the elucidation of dental disease a fuller knowledge of the bacteriology of the oral cavity is essential. Whether this object can best be obtained by training men with a dental qualification and a special knowledge of the dental tissues in bacteriology later or whether it would be a better investment to train fully qualified medical bacteriologists in the special requirements of the dental surgeon is a debatable point. Personally I think that the best result would be obtained by the first method. A knowledge of the basic sciences which give that foundation on which pathology is based is essential. A study of the dental diseases would bring many blessings to mankind.

Like the microbe hunters of long ago I am confident that there will arise a younger more inquisitive generation than mine who will bring to this study of the dental diseases the same skill and enthusiasm as was shown by Pasteur and Koch.

"They say my verse is sad; no wonder
Its narrow measure spans
Tears of eternity and sorrow
Not mine but man's
This is for all ill-treated fellows
Unborn and unbegot
For them to read when they're in trouble
And I am not."—*Laurence Housman.*

BIBLIOGRAPHY

BANTOCK, G. G. (1899) The Modern Doctrine of Bacteriology or the Germ Theory of Diseases. London.
BEATTIE, J. M. (1913) *Lpool med.-chir. J.*, **33**, 33.
BULLOCH, W. (1938) The History of Bacteriology. London.
GRENNAN, S. (1946) *Brit. dent. J.*, **80**, 274.
GOADBY, K. W. (1903) The Mycology of the Mouth. London.
—— (1922) Diseases of the Gums and Oral Mucous Membrane. London.
JAY, P., CROWLEY, M., HADLEY, F. P., and BUNTING, R. W. (1933) *J. Amer. dent. Ass.*, **20**, 2030.
DE KRUIF, P. (1927) The Microbe Hunters. New York.
LEBER, T., and ROTTENSTEIN, J. B. (1878) Dental Caries and its Causes. Translated by H. Chandler. London.
LEDLINGHAM, J. C. G. (1944) *Brit. med. Bull.*, **2**, 261.
LINDSAY, L. (1929) *Brit. dent. J.*, **50**, 1289.
LUFKIN, A. W. (1948) A History of Dentistry. 2nd ed., London; pp. 225–6.
MACKIE, T. J. (1923) *Brit. med. J.*, ii, 1241.
PETRIE, G. F. (1943) *Nature, Lond.*, **152**, 683.
WEINBERGER, B. W. (1948) Introduction to the History of Dentistry in America. St. Louis; vol. 2.
WOODHEAD, G. S. (1897) *Practitioner*, **58**, 675.

Section of Psychiatry

President—E. B. Strauss, M.A., D.M., F.R.C.P.

[*October* 13, 1953]

Moral Responsibility and the Law

PRESIDENT'S ADDRESS

By E. B. Strauss, M.A., D.M., F.R.C.P.

Introduction

The title of my Address, Moral Responsibility and the Law, will immediately cause discomfort in the minds of those psychiatrists who believe that a psychiatrist should be so detached from a philosophy of values and from moral considerations of all kinds as to be able to practise his art and science in a kind of moral vacuum. Nevertheless, it has always been my contention that no doctor (whether he practises psychological medicine or any other branch) can afford to adopt a position of such artificial isolation without running the risk of losing touch with reality.

Furthermore, a physician, in spite of certain social privileges, such as exemption from serving on a jury, to which he has attained over the centuries, remains an ordinary citizen and has the right and the duty to contribute the weight of his professional experience towards the solution of problems affecting the commonweal. It is for that reason that the various Royal Commissions which have considered capital punishment have always seen fit to take evidence from representative medical men and women, acting as individuals or as delegates of professional associations. For example, the last Royal Commission on Capital Punishment, under the Chairmanship of Sir Ernest Gowers, accepted memoranda both from the British Medical Association and from the Royal Medico-Psychological Association and heard the evidence of their deputed witnesses.

It is the psychiatrist, perhaps, who is more concerned with medico-legal problems when it comes to capital offences than any other doctor. The Prison Medical Officer, who invariably gives evidence in murder trials, need not have had any special training in general psychiatry; but it often happens that his evidence is more to the point and more acceptable to the judge and jury than that given by the specialist in psychological medicine.

My approach will be largely historical and philosophical. I shall support one main thesis only: the durability and value of any civilization or organized culture-pattern depend on the moral basis of the system of Common Law which has been established. In other words, a system of law that is not firmly rooted in a sound morality gives rise to features which will eventually cause a society to crumble. Our civilization, for instance, endures because the law is so greatly respected; and the law is respected in virtue of its conformity with the Moral Law.

However, the public conscience, anyhow for the past century, has been particularly delicate and sensitive so far as capital punishment is concerned; and many thoughtful and responsible citizens have come to believe that the M'Naghten Rules, as at present formulated, to a certain extent undermine the moral basis of the Common Law.

It is because I believe that the slight modification of these rules, with the addition of an extra "limb", as recommended by the Council of the B.M.A. in its memorandum to the Royal Commission, would serve to bring things up to date and satisfy our social conscience, that I would support those changes.

Historical Background

Although in England there was some kind of conception of man being free and responsible before the middle of the thirteenth century, it was, so far as one can tell, poorly reflected in the administration of justice; and, in practice, the relationship between the common man and his overlord was very much a slave-master relationship.

It was perhaps not until 1258, when Henry of Bracton wrote the first legal textbook that the Common Law of England came to be firmly based on the moral idea. This remarkable man was a priest, a Chancellor of Exeter Cathedral and a Judge. His textbook was entitled "De Legibus et Consuetudinibus Angliæ". His notion of guilt has its roots in moral theology, with its insistence on *mens rea* (the intentionally guilty mind) as the criterion. He stated that *Rex est sub deo et sub lege* (the King is subject to God and to the Law); and all his legal formulations were based on the idea of *liber et legalis homo* (free and responsible man). He also wrote: *de omni homine præsumitur quod sit bonus homo donec probatur in contrarium* (it is the right of every man to be considered a good man unless it can be proved to the contrary).

An analysis of Bracton's sources shows that they included Greek and Roman texts, the Hebrew Old Testament, the New Testament, Saint Augustine and both early and contemporary Canonists, amongst whom was Saint Raymond of Penafort, who was the Dominican Master General. This cleric insisted on a distinction being drawn between *actio humana* (the act of a responsible, integrated human being) and *actus hominis* (the deliberation as such, regarded independently of the agent); this concept is, of course, directly referable to the rudimentary psychology of " self-examination".

Chief Justice Fortescue in the fifteenth century wrote two important treatises in the same tradition: "De Laudibus Legum Angliæ", and "De Monarchia". He derived many of his ideas from Aristotle, St. Augustine and St. Thomas Aquinas.

Christopher St. Jermyn in the sixteenth century published his "Law and Equity", in the form of a dialogue between a doctor of theology and a student of law. He was in close touch with Chancellor Gerson of Paris University; and his approach was again that of the Catholic Humanist. Sir Thomas More, one of England's greatest Lord Chancellors, was, of course, exactly in the same tradition—Aristotelian and Thomist.

Although the Catholic-Humanist tradition was broken from the sixteenth century onwards, the library of Sir Edward Cooke, a Protestant, was stacked with books of divinity, including the works of St. Thomas Aquinas and St. Augustine; and he stated categorically that the Law of England is based upon the Law of God.

It is interesting to note that as late as 1579 one in three of the practitioners of Law in the Temple were known Papists. Thus, from the Reformation onwards we have the paradox of the old Christian, as opposed to the secular, tradition being carried on by lawyers—Protestant as well as Catholic—rather than by the Clergy.

In other words, it would seem, then, that the collective conscience of the British people has been formed and informed by Christian Ethics and that, over the centuries, we have come to owe our conception of justice to the Common Law rather than to more narrowly religious formulations.

It was perhaps Thomas Hobbes, the first great secularist, who in the seventeenth century began to throw doubt on the moral basis of law. You will remember his dictum that "the life of man in his natural condition is solitary, poor, nasty, brutish and short". Hobbes and his sympathizers concluded as a natural corollary that the natural man must be coerced.

It is not too fanciful, I think, to regard this line of thought as providing the foundation stone of the totalitarian states of our own era. In parenthesis, I might say that the pessimism of Hobbes' aphorism can only be equalled by that of the late Dr. David Eder: "We are born mad. We acquire morality, and become stupid and unhappy. Then we die." It is interesting to note that Hobbes' chief opponents were lawyers, such as Lord Clarendon and Sir Matthew Hale; and Sir Henry Finch in 1687 in his "Description of the Common Law in England" maintained that the principles governing the law are to be derived from all the sciences, legal and "foreign", i.e. non-legal. He described these sources in the following words "out of the best and very bowels of Divinity, Grammar, Logic, also from Philosophy, natural, political, economical, moral, though in our Reports and Year Books they come not under the same terms, yet the things which you find there are the same; for the sparks of all the sciences in the world are raked up in the ashes of the law".

In the words of Holdsworth: "The general rule of the common law is that crime cannot be imputed to a man without *mens rea*. It is, of course, quite another question how the existence of that *mens rea* is to be established. The thought of man is not triable by direct evidence; but if the law grounds liability upon intent it must endeavour to try it by circumstantial evidence. Much of that circumstantial evidence will be directed to show that a man of ordinary ability, situated as the accused was situated, and having his means of knowledge, could not have acted as he acted without having that *mens rea* which it is sought to impute to him. In other words, we must adopt an external standard in adjudicating upon the weight of the evidence adduced to prove or disprove *mens rea*. That, of course, does not mean that the law bases criminal liability upon non-compliance with an external standard. So to argue is to confuse the evidence for a proposition proved by that evidence."

In so far as this Address can ultimately be limited to a consideration of the desirability of retaining the M'Naghten Rules as at present formulated, in the light of modern mental science, the question resolves itself as follows: do the M'Naghten Rules provide a sound criterion for the establishment of *mens rea* (the intentionally guilty mind), especially in capital offences?

Philosophical Background and the Nature of Law

However, before I do this, I should like to outline the philosophical background against which I have tried to review the problems suggested by the title of my Address, "Moral Responsibility and the Law". The position that I am assuming is, roughly speaking, Thomist and may be considered as taking up a midway stand in between idealist, ethical formalism and stoicism on the one hand and mere utilitarianism on the other.

According to such a viewpoint, social morality may be said to lie between the extremes of anarchism and collectivism. In this context, anarchism is meant to imply such an insistence on the dignity of the individual that group-values may in certain circumstances be defied. Collectivism assumes exactly the opposite, i.e. that the individual is to be regarded merely as a unity who possesses significance only in relation to the mass.

Let me briefly consider the concept of law before more closely examining some of the philosophical implications of moral responsibility.

Law is an analogical term, with varying, though related, meanings for the moralist, the lawyer and the natural scientist, whether the last-mentioned be a physicist or a physician. For the moralist, the law is significant on four main counts: (1) as an ordinance of reason which is (2) issued by the competent authority (3) for the sake of the common good and (4) promulgated to those who should obey it.

It is to be noticed that four important elements stand out in this definition: (i) law is not a dictate of power, although the ability to enforce it is assumed, but rather a statement charged with intelligence. (ii) Law is not just a personal precept, deriving from some private authority or other, such as one's father, spiritual director or psychiatrist. (iii) Its direct purpose is a "whole happiness" which must (iv) make sense in the minds of those who are subjected to it.

This moral-theological notion of the law is based on the conviction that the world is governed by intelligence, and that we are all sufficiently akin for general statements to be made about us. In other words, the notion breaks down if it is assumed that we all stand on our own merits and that every individual is to be regarded as a special case.

If my short historical survey of the origins of our Common Law be substantially correct, it will be seen that experts in both Common and Canon Law have over the centuries accepted a definition of law such as I have just given. In other words, they have been content implicitly to build on foundations which depend on the moral idea, although the lawyers themselves seldom make explicit reference to morality as such. In fact, they, like doctors or any other specialists, can be very suspicious of moral dicta—and rightly and properly so in certain circumstances.

Nevertheless, a lawyer, who reflectively harks back to his premises, finds himself, willy-nilly, engaging in philosophical speculations. He will ask himself, for instance, whether there is such a thing as a Natural Law, a δίκη, antecedent to his own discipline. Of recent years, it must be admitted, legal philosophers were apt to reject theories which assumed the existence of a Natural Law. However, the belief that the Natural Law exists in a very real sense and gives substance to civilized codes is again coming into favour, and has, as indicated earlier in my Address, always been nobly defended by great lawyers, implicitly assumed in the Common Law of England and applied by the most able judges.

Law for the natural scientist may be a quasi-mathematical statement, expressing a statistical relationship or co-ordinating explanatory hypotheses; or it may represent a semi-poetical exposition of Nature's august impersonality. However, since it is not applicable to human behaviour-patterns exclusively, we may leave it on one side.

The psychiatrist, in view of the nature of his work, must of necessity accept the notions of law which are shared by the moralist and the lawyer: the moralist, because of his concern with what a person *ought* to do in order to be happy; the lawyer, because his main interest is in the field of the individual's smooth adjustment to his social environment.

At this stage, it would be useful, I think, to recapitulate this philosophical position in more formal language. It is a position which depends on dogmatic theology, it is true; but it is one which is as well worth stating as that assumed by exponents of the entirely secular state.

Above, behind and interwoven with every law, the Eternal Law, the *Lex Æterna*, which exists in the mind of God, is to be discerned. This is the Logos, the Verbum, which is identified by the Christian theologian with the Second Person of the Trinity, who is thought of as the exemplar, the first agent and the purpose of every statement that makes sense. As a derivative therefrom, in the mind of every rational creature without the interposition of human authority, we have the Natural Law, the *Lex Naturalis*. The word "natural" is not used here in contrast to "supernatural", but rather in the sense of the obverse of "artificial". The Natural Law represents a body of rules which should in theory be self-evident, although in practice they are often not so.

In so far as some of these rules are in the nature of primary principles, they are fairly evident. Others are more like conclusions, which are debatable. For example, it is more obvious that a husband should cherish his wife than that he should cherish only one at a time.

The theologian would claim that the Natural Law includes an obligation to serve the community, which raises the question of what exactly society demands of the citizen. The community does not make a simple statement that he should observe the Natural Law, but proceeds to try to settle (and, in a sense, somewhat arbitrarily) points which are at the time considered necessary for the maintenance of respect for the Natural Law and, perhaps more conspicuously, essential for the preservation of public peace and safety. At this point we encounter what the Thomist philosophers call the Positive Law or *Lex Humana*.

The regulations which come under the Positive Law originate in the Eternal Law, but the dialectical process is different from that of the Natural Law. For, whereas the precepts of the Natural Law can in a sense be deduced from their premises (for example, one can infer that monogamy provides the best way of promoting a happy and stable man-woman relationship), those of the Positive Law are, as it were, constructed and imposed, and derived from an act of legislative will. Alternative courses may be open, but the competent authority has to decide on one or the other for the sake of uniformity; and the decision, provided that it does not contravene the Natural Law, is held to be just and binding.

It is to be noted that the concept of the Natural Law is rather a woolly one unless it is seen against a background of dogmatic theology, when it becomes crystal-clear; but, for that very reason, the notion may be repellent to a modern audience. Let me repeat again, however, that the position must be stated in view of the fact that the Common Law of England is a direct derivative therefrom which has inevitably helped to form what may be called the Collective Super-Ego in these Islands.

The Positive or Human Law is represented in the case of the State, or political community, by the Civil Law; for the Church (here regarded as a visible corporation and not as a mystical body) it is embodied in the Canon Law.

The chief test of the differences between the Natural Law and the Positive Law is as follows: in the case of the former, certain acts are considered good and therefore commanded; others are considered bad and hence forbidden. In the case of the Positive Law, the position is reversed: certain acts are commanded and therefore considered good; others are forbidden and therefore regarded as bad.

The distinction is not to be thought of as a division of watertight compartments, although some theorists on both sides have treated it as such. Thus, there are moralists who regard natural and religious precepts as being the only really binding laws, and the demands of the Civil Law as merely *penal*. Thus, if you infringe the Customs regulations and are found out, you have to pay the price, and cheerfully. Representing the other point of view, there are secular lawyers who state that moral and religious condemnations are just private considerations, which may or may not be respected by the sovereign civil authority. I have no wish to enlarge upon this, but it does give a hint of the conceptual difference between *Sin* on the one hand and *Crime* on the other, thereby providing a useful safeguard.

Every deviation from the law, i.e. the right course of action, was originally termed sin, *peccatum*; but, with the development of complex, organized juridical communities (of Church and State) it came to be recognized that there were times when it was one thing to disobey the moral law and another to attract the attention of the police.

It was further realized that it was no part of the duty of the State school-marmishly to legislate for every twist and turn of the Natural Law, and that it would be intolerable if it tried to make every sin into a crime. Conversely, with due regard for the duty of obeying our superiors, there is a defensible humour in the religious hesitation to treat every crime as a sin.

The Natural Law, then, tends to be more interior, subtle and non-compulsive than the Positive Law, which is more exterior to the self and, in a sense, stiffer and more minatory. The theologian would claim that God alone can search the heart of man and judge culpability with any certainty. Human judges have to be guided by the Positive Law; and, though a just system of law will take motives into account, its enquiry will stop short of imputing sin in a theological sense. That is one of the reasons why I personally find moral homilies and condemnations from the Bench so out of place and distasteful.

Moral Responsibility

I shall consider very briefly the question of *Moral Responsibility* against the same kind of background. Responsibility means different things to the theologian and to the lawyer; and I should imagine that the psychiatrist finds himself occupying a rather uncomfortable position in between the two.

The theologian has two roles to fill: that of the theorist and that of the practitioner. As a theorist, he teaches moral theology; as a practitioner, he administers the Sacrament of Penance and acts as a spiritual director. According to theology, grave sin represents a failure to enact a good which it was realized was greatly worth doing, and which in the circumstances positively required to be done, with the presupposition that it was known to be a failure and that the failure was deliberate; or, expressed in slightly different language, full consent and deliberation were involved. The act may be wrong in itself, but the guilt lessens in proportion to the ignorance and lack of deliberation. It is interesting to note that these categories are exactly reflected in the M'Naghten Rules.

However, when it comes to dealing in practice with the penitent, in other words, when the confessor acts as judge, he is at once more cautious and more slap-dash—more cautious, because he knows that God is the sole judge of consent and deliberation; more slap-dash, because God is not a criminal investigator and does not demand a close analysis.

The Civil Law, because it is more wooden, has to be more circumspect. It may be trying a man for his life. According to the law, it has to be proved beyond reasonable doubt that the crime has been committed, that the law was known or should have been known to the accused, and that the act was done deliberately with consciousness of its illegality. Clearly, the M'Naghten Rules are an echo of theology; and a theologian may well feel that it would be difficult to improve them substantially. May I remind you of the M'Naghten Rules as at present formulated: according to the M'Naghten Rules, to establish a defence on the ground of insanity in a criminal case, "it must be clearly proved that, at the time of the committing of the act, the party accused was labouring under such a defect of reason from disease of the mind, as not to know the nature and quality of the act he was doing, or, if he did know it, that he did not know he was doing what was wrong".

The psychiatrist is in a less happy position, and for the following reasons: (i) his main concern is to cure his patient rather than to "liquidate" him. (ii) If he has any humility at all, he has less confidence in his *métier* than the theologian has in his. (iii) He is not in a position confidently to leave his patient to God's Providence. (iv) As he is not directly a servant of the State, he rightly feels that his main concern is with the welfare of his patient and that he can leave it to other people to look after the interests of society. For these reasons and many more, unless he takes very great care, the evidence given in Court by an independent psychiatrist, acting as an expert witness, may easily be biased, muddled and irrelevant. In fact, many lawyers delight in bringing all these charges against the psychiatrist. Nevertheless, it would be universally agreed that the lawyer, the theologian and the psychiatrist must take the important principle of *Equity* into account. Equity acts in favour of the spirit of the law as against its letter; and if it can be shown that in many instances the M'Naghten Rules operate in opposition to equity, a strong case can be made for their revision.

If it can be further demonstrated that, in the light of modern knowledge, the M'Naghten Rules in their present formulation violate the letter as well as the spirit of the law, the case for their revision becomes even stronger; and it is my belief that the Rules are an offence both in Law and in Equity.

It is interesting to note that Sir Walter Moberly in his Riddell Memorial Lectures on "Responsibility", relying almost exclusively on non-Catholic sources and authorities came to very nearly the same conclusions on the question of moral responsibility *vis-à-vis* the law as I have done.

It will be remembered from my little historical survey of the problem that it is an inalienable principle of Common Law that a man can be found guilty of the offence with which he is charged and punished accordingly only if *mens rea* (the intentionally guilty mind) can be established in accordance with the currently acceptable rules of evidence. It is clearly impossible to establish *mens rea* in the case of an insane person, for an insane person is held in law to be irresponsible. That is one of the reasons why amongst the recommendations put forward by the B.M.A. there was one to the effect that the wording of the verdict, "guilty, but insane" be changed. The memorandum suggested that the wording should be amended to read roughly as follows: "the accused did the act (or made the omission) with which he is charged, but is not guilty on the ground that he was insane, so as not to be responsible at the time, according to law". Let me again insist that the concept of guilt is valueless unless it presupposes moral responsibility in the guilty person; and a person judged to be insane in respect of a certain act is irresponsible and hence cannot possibly incur guilt.

The problem can therefore be reduced to the following question: do the M'Naghten Rules serve as the best possible instrument for the establishment of insanity in open Court, or can they be improved?

Before I summarize the arguments in favour of the revision of the M'Naghten Rules and the recommendations of the B.M.A. given in evidence before the Royal Commission, I should like to put another rhetorical question and provide an answer expressed in psychological language: what is all the fuss about, seeing that, on an average, not more than a dozen people are hanged in the course of a year in Great Britain?

The "Collective Super-ego"

In my opinion, it is legitimate (by analogy, be it noted) to make use of a concept which may be termed the "Collective Super-Ego" which is to be regarded as the unconscious counterpart of the social (or collective) conscience.

In the case of the individual patient, we know from our psychiatric experience that tensions which are dangerous for mental health develop when there is too great a discrepancy between the unconscious conscience (the super-ego of the Freudian schema) and the more "adult" moiety of the conscience which is informed by the intellect. We know, for instance, that discrepancies of that kind may contribute ætiologically to obsessive-compulsive neurosis, to psychogenic anxiety-states, depressive syndromes and paranoid reaction-formations.

It seems to me that the same principles apply to the social collectivity. Jung realized this although he employed different concepts and made use of a different terminology to express it.

In Nazi Germany the laws of the Reich were altered overnight in such a way as to satisfy the most disreputable demands of the instincts (in favour of the Id, as the psychoanalysts would put it), with the result that an unbridged gulf developed between the social conscience and the Collective Super-Ego, which inevitably remained unchanged and which was still largely a compound of Christian ethics. We know what followed: deliria, unbridled aggression, savagery, panic, mass paranoia and finally despair.

In other totalitarian regimes the social conscience sanctions the "liquidation" of political opponents on the grounds that they are "enemies of the State" and have thereby forfeited their right to live. We do not know, even after thirty-five years, whether the Collective Super-Ego of these peoples has caught up on the social conscience and finally dragged it away from its roots in the soil of the Natural Law. There is much to suggest that it has not. In England to-day it is common for even kindly and educated people to say, for example: "What is the use of keeping creatures like Straffen alive? Monsters, such as Haigh or Heath, even if some sentimental and woolly-headed psychiatrists may care to regard them as insane, are better dead; if kept alive, they are only a burden on the State and a misery to themselves". Or again: "Idiots and imbeciles should be painlessly put to death at birth or shortly afterwards". We have our distinguished and enlightened supporters of euthanasia, "mercy-killing" (so-called) and sterilization for eugenic or other social considerations. In Denmark, a highly civilized, but entirely secular, State, the law permits of the "voluntary" castration of psychosexual deviants.

It may be thought that in England we are still a long way from the Nazi practice of emptying the mental hospitals and institutions for mental defectives by transferring their occupants to the gas chambers; but, in my opinion, the dividing line is a thin one. In those days in Germany a psychiatrist who signed a certificate of lunacy or mental defect knew full well that he was likely to be signing a death warrant. I have since spoken to colleagues in Germany who had broken down under the strain.

The general public in Great Britain—anyhow its more sensitive and educated members—has come to realize obscurely that, in the light of modern mental science, the M'Naghten Rules do not necessarily establish moral irresponsibility, which is the only aspect of insanity with which the Law need concern itself in this connexion. That fact is for me a sure sign that there is a cleavage between the conscious elements of the changing social conscience and those largely unconscious components which I have called the Collective Super-Ego; and I believe that the situation which has been allowed to develop is dangerous from the point of view of mental hygiene.

Arguments for Revision of the M'Naghten Rules

The Minutes of Evidence taken before the Royal Commission on Capital Punishment, No. 14 on February 3, 1950, outline the chief arguments raised in favour of a revision of the M'Naghten Rules. The Rules, it will be remembered, equate disease of the mind with a defect of *reason*. When these rules were formulated a hundred years ago, a man was regarded as a kind of reasoning machine; in other words, the psychology of those times took note of the intellect only and remained unaware of any of the principles governing man's emotional life in health and disease. Insanity, therefore, of necessity involved a "defect of reason".

To-day we know, however, that many forms of insanity—in fact, most kinds—do not primarily impair the intellect so much as disorganize the life of the emotions, and in such a way as to deprive a man of his capacity for moral choice, or anyhow seriously to distort his perceptions of right and wrong.

This extended concept of insanity should, therefore, in the light of modern, well-established mental science, be recognized in Common Law, as it is in clinical psychiatry.

For example, I can readily recall the case of a young murderer who could and should on many occasions, in appropriate circumstances, have been certified as of unsound mind. The M'Naghten Rules in their present form made it impossible for his counsel successfully to establish a verdict of "guilty but insane"; nor, after the usual statutory enquiry, was the prerogative of mercy invoked in this case.

Examples of abnormal mental states which fail, in very many instances, to be covered by the M'Naghten Rules, if the rules be strictly interpreted, include: aggressive psychopathic states; states of mind associated with organic damage to, or disordered physiological functioning of, the brain; melancholia in one or other of its many forms; early schizophrenia (or dementia præcox, as it is sometimes called); and delusional insanity.

Another very important argument in favour of the revision of the M'Naghten Rules is the fact that the various judges interpret them in accordance with their own assessment of the individual case, which may be good in equity but is bad in law. Until Lord Chief Justice Reading ruled that the word "wrong" was to be interpreted as meaning "against the law", a wider interpretation was permissible. However, humane judges even now see fit on occasions to disregard Lord Reading's ruling. The following is a case in point:

A young man was recently put on trial for strangling his sister. He had promised his mother on her death-bed that he would look after his sister after her death. This man was, in my opinion, suffering from the depressive form of schizophrenia, which I called "Melancholia" in order not to fog the judge and jury unnecessarily. He had the delusion that his father was likely to die very shortly and that he

himself had not got long to live. It seemed to him, therefore, that there would be no one left to look after his sister and that it was his moral duty to kill her. Throughout he was fully aware of the nature and quality of his act and knew that it was against the law and punishable by death. Nevertheless, he was convinced that his act was not only morally justifiable but inevitable; in fact, he told me that in the same circumstances he would do the same thing over again; nor did he wish to escape the consequences by pleading insanity. The judge, in his summing up, directed the jury to return a verdict of "guilty but insane", which they did without leaving the box.

Another judge who might have regarded Lord Reading's ruling as binding would rightly and properly have directed the jury otherwise. The chances are that, after a statutory enquiry, the prerogative of mercy would have been invoked, but not before the death sentence had been pronounced in open Court with all the awful solemnity and ceremonial that accompany these occasions.

Up till now, the M'Naghten Rules have not been held to cover cases of mental deficiency, however severe. The B.M.A. Memorandum commented on this as follows: "The first question is as to the meaning of 'disease of the mind'. The Select Committee on Capital Punishment which reported in 1930 thought that it was desirable to 'extend the area of criminal irresponsibility in the case of the mentally defective'. It may be that mental disease is commonly understood to include mental defect, but the Association suggests that it should be clearly laid down that 'disease of the mind', as used in the definition of irresponsibility, covers incomplete mental development as well as grave disturbances of mental health."

The Recommendations of the British Medical Association to the Royal Commission

The B.M.A. recommended that the M'Naghten Rules should be amended to read more or less as follows:

(A) To establish a defence on the ground of disease of the mind, the party accused must prove that, at the time of committing the act, he was labouring, as a result of disease of the mind, under
  (1) a defect of reason such that he did not know
    (*a*) the nature and quality of the act he was doing; or (if he did know this)
    (*b*) that he was doing what was wrong; or
  (2) a disorder of emotion such that, while appreciating the nature and quality of the act, and that it was wrong, he did not possess sufficient power to prevent himself from committing it.

Note.—(*a*) "Disease of the mind" covers incomplete mental development as well as grave disturbances of mental health. (*b*) "Wrong" means, not "punishable by law", but morally wrong in the accused person's own opinion.

(B) When a jury find that an accused person, at the time of the committing of the act, was labouring, as a result of disease of the mind, under a defect of reason or a disorder of emotion to such an extent as not to be fully accountable for his actions, they shall return a verdict of "guilty, with diminished responsibility".

The report of the Royal Commission has been published to-day (i.e. at the time of writing); and the Commission recommends that the M'Naghten Rules be amended to read as follows: "The jury must be satisfied that, at the time of committing the act, the accused, as a result of disease of the mind or mental deficiency (*a*) did not know the nature and quality of the act, or (*b*) did not know that it was wrong, or (*c*) was incapable of preventing himself from committing it."

In a carefully reasoned argument the Report gives its reasons for failing to recommend the adoption in English Law of the Scottish practice in relation to a verdict of "guilty, but with diminished responsibility".

It would seem, then, that, in the main, the principles that I have advocated have been found acceptable by the majority of the Members of the Royal Commission on Capital Punishment, and that medico-psychological opinion has played a large part in bringing this about.

Nevertheless, recommendations of Royal Commissions require to be endorsed by Parliament in order to become effective; and this often fails to happen.

It is, however, my hope that this Address may, even in the smallest of small ways, influence the "climate" of psychiatric opinion in the desired sense, and that the change may be reflected in wider circles.

PRINCIPAL SOURCES

GIBBY, T. (1953) Between Community and Society. London; and Personal Communication.

HAWKINS, D. J. B. (1948) Punishment and Moral Responsibility. In: The King's Good Servant; Papers read to the Thomas More Society of London. Oxford.

Minutes of Evidence taken before the Royal Commission on Capital Punishment (1949–50). H.M.S.O. London, 1953.

MAYBERLY, W. (1951) Responsibility; Riddell Memorial Lectures. London.

O'SULLIVAN, R. (1950) The Inheritance of the Common Law. London.

— (1953) Personal Communication.

BOOK RECEIVED FOR REVIEW

(As no reviewing is undertaken in the "Proceedings" this is the only acknowledgment made of books received for review)

Sophian (J.). Toxæmias of pregnancy. pp. 231. London: Butterworth. 25s. 0d. 1953.

BOOKS RECENTLY PRESENTED AND PLACED IN THE SOCIETY'S LIBRARY

Birch-Jensen (A.). Congenital deformities of the upper extremities. pp. 285. Odense: Andelshogtrykkeriet i Odense & Det danske Forlag. Dan. Kr. 25 (35s. 0d.). 1949.

Busscher (J. de), and **Scherer (H. J.).** Les gliomes de l'encéphale. pp. 160. Tome I. Brussels: Edition Universelle, S.A. 1942.

Claye (A. M.). A short history of the Hospital for Women at Leeds, 1853–1953. pp. 40. Leeds. 1953.

Committee for the Study of Nursing Education. Nursing and nursing education in the United States. pp. 585. New York: Macmillan. 1923.

Erlacher (P. J.). Die Technik des orthopädischen Eingriffs: eine Operationslehre aus dem Gesamtgebiet der Orthopädie. pp. 482. Vienna: Springer. 1928.

Hemley (S.). Orthodontic theory and practice. 2nd edit. pp. 592. New York: Grune and Stratton. $14.50. 1953.

Iason (A. H.). Gastric cancer. pp. 316. New York: Grune and Stratton. $7.50. 1953.

Jaschke (R. T. v.). Lehrbuch der Geburtshilfe. 4te Aufl. pp. 770. Berlin: Springer. 1935.

Jaschke (R. T. v.), and **Pankow (O.).** Lehrbuch der Gynäkologie. 5te Aufl. pp. 759. Berlin: Springer. 1933.

Lamy (M.). Les applications de la génétique à la médecine. pp. 145. Paris: Doin. Fr. 122. 1944.

Lewis (R.), and **Maude (A. E. U.).** The English middle classes. pp. 320. London: Phœnix House. 15s. 0d. 1949.

Myburgh (A. L.). Causes and treatment of abdominal adhesions. pp. 184. Leiden: Eduard Ijdo. 1953.

Nissen (R.). Chirurgische Indikationen. pp. 177. Leiden: Sijthoff. 1937.

Paula e Silva (J. de). Hematologia aplicada. pp. 512. Saõ Paulo: Edigraf. 1945.

Rhéaume (P.). Technique chirurgicale: estomac et duodénum. pp. 260. Paris: Masson. Fr. 50. 1932.

Schmidt (K. E. A.). Laparoskopische Tafeln. Grenzach: Deutsche Hoffman-La Roche A.G. *ca.* 1952.

Société des Sciences Médicales de Tunisie. Médecine and médecins de Tunisie de 1902 à 1952. pp. 335. Tunis: Société des Sciences Médicales de Tunisie. 1952.

Sophian (J.). Toxæmias of pregnancy. pp. 231. London: Butterworth. 25s. 0d. 1953.

Veau (V.). Division palatine: anatomie, chirurgie, phonétique. pp. 568. Paris: Masson. Fr. 600. 1931.

Wall (O. A.). Sex and sex worship (phallic worship). pp. 608. St. Louis: C. V. Mosby Co. 1920.

Zijlstra (W. G.). Fundamentals and applications of clinical oximetry. 2nd edit. pp. 150. Assen: Van Gorcum. Fl. 11.00. 1953.

Section of Physical Medicine

President—DORIS BAKER, M.D., F.R.C.P.

[*October* 14, 1953]

DISCUSSION ON SPONDYLOSIS

Dr. A. C. Boyle (Middlesex Hospital, London): *The Pathology and Incidence of Spondylosis.*

For many years, the radiological finding of osteophytosis of the spine was reported as being a manifestation of osteoarthritis, and clinicians were satisfied with this diagnosis. Recent knowledge suggests that this term should include only those patients who have radiological evidence of arthritic change in the spinal apophyseal joints, and special oblique radiographs are necessary to demonstrate these changes with certainty.

If these cases be excluded, there is left a large group of patients in whom radiography of the spine discloses the formation of osteophytes on the anterior and lateral borders of the vertebral bodies, associated with a greater or lesser degree of narrowing of the intervertebral discs, and occasionally calcification or ossification of the intervertebral ligaments.

It is probably true to say that the rejection of the diagnosis of osteoarthritis in these cases is now acceptable to the majority, but the latter term has been replaced by a variety of names, some of which relate to different stages in a progressive pathological process. Among the many names applied to the condition are:

Hypertrophic spondylitis (American authors)
Spondylitis osteoarthritica (Knaggs)
Spondylitis deformans (Benecke)
Spondylosis deformans (Schmorl)
Spondylosis
Spondylarthrosis (American authors)
Polyspondylitis marginalis osteophytica (Shore)
Disc degeneration
Discopathy
Osteophytosis (Collins)

Of this bewildering variety of names, the last is probably the most satisfactory, for it is a simple and accurate description of the major visible pathological change, and presupposes no specific ætiological factor.

PHYSIOLOGICAL AND PATHOLOGICAL CHANGES IN DISC TISSUE

That the condition is primarily due to change in the intervertebral discs is now acceptable to many, but before attempting a description of the pathological changes which take place, it is well to bear in mind the physiological change which takes place in this structure with advancing years. We should perhaps also bear in mind the fact that the dividing line between the physiological and the pathological

in this, as in many other conditions, is by no means clear cut, normality and morbidity merging almost imperceptibly and being a matter of degree rather than of kind.

The structure of the intervertebral discs at known ages has been studied by, among others, Keyes and Compere (1932), Coventry *et al.* (1945) and Peacock (1952). The latter author studied fresh post-mortem specimens of lumbar discs from 30 subjects, ranging from full term to 80 years of age, who were, as far as was known, free from spinal disease or deformity. At full term, the disc is described as being biconvex and of considerable thickness, the vertical height being almost one-half that of the adjacent vertebral bodies. The nucleus pulposus is large, and in the sagittal plane occupies about one-half of the antero-posterior diameter of the whole disc. The shape of the nucleus pulposus is quadrilateral, and it appears to be composed of a homogeneous substance containing scattered clumps of cells. Microscopically, the nucleus pulposus is formed by a mass of homogeneous, mucoid substance, in which are seen at intervals the remains of a chorda-reticulum. The chorda-reticulum is formed by intercellular spaces containing mucoid substance, some cells being compressed into large tracts, others being isolated as small clumps. Notochordal tissue appears to be absent after 10 years of age.

The distinction between the annulus fibrosus and the nucleus pulposus is quite clear, and it is the gradual loss of this distinction which is one of the earliest changes of the ageing process, being apparent from the age of 21 onwards. At this age, the tissue of the nucleus appears less translucent, and though it is of markedly gelatinous character, it is of a firmer consistency. With the advance of age, the fibres of the annulus become coarsened and hyalinized, while in the nucleus, the notochordal element is replaced by fibrocartilage. Later, the fibrocartilage of the nucleus, at first delicate and containing much fluid, becomes progressivly coarsened and desiccated. Desiccation also occurs in the disc as a whole, especially after 30 years of age, but it is more marked in the nucleus than the annulus.

At 75 years, the distinction between the nucleus and the annulus is difficult, but the nucleus still has a softer consistency than the annulus. Cleft formation is seen in the disc, horizontal fissuring extending almost completely through the disc. The nucleus itself is of coarse fibrocartilage, and remains avascular. Peacock concludes, as do other authors, that the incidence of true herniation of the nucleus pulposus would diminish with advancing age.

Collins (1949) gives the water content of the nucleus pulposus as 88% at birth, falling to 70% in old age. He also stresses that desiccation of the disc is an important cause of its narrowing, and that this narrowing is accelerated if blood vessels from the vertebral marrow penetrate the cartilage end-plates and ramify within the disc. He describes fissuring and fibrillation of the fibrocartilage as being a common finding in the elderly, a change which may be accompanied by the deposition of an unidentified brownish pigment, a process named by Schmorl "brown degeneration". Collins goes on to describe the important consequences of degeneration of the discs, and relates this change to the spinal osteophytosis which is such a common radiological finding. Among the consequences of disc degeneration he mentions diminution of spinal movements, and forward tilting of the vertebræ, leading to marked spinal kyphosis. This imbalance throws abnormal strains upon the posterior apophyseal joints, predisposing them to osteoarthritic change. Marginal osteophytes are a relatively late development, forming on the anterior and lateral borders of the vertebral bodies.

Collins also clearly describes the mechanism of formation of these osteophytes. The daily trauma of activity gives rise to compression by the adjacent vertebral bodies upon the fissured and desiccated disc, causing the forward protrusion of its degenerated components. This forward protrusion cannot, however, take place directly in the mid-line, being limited by the anterior common ligament, but on either side of this ligament the degenerated disc is pushed forwards and lifts the periosteum from the vertebral body, new bone being formed beneath the area of periosteal elevation. This new bone is at first compact, but later becomes cancellous, and will then contain marrow spaces which are in communication with the general marrow cavity of the vertebra. In the lumbar and dorsal spine, osteophytes rarely form on the posterior margin as the collapsed disc is always compressed forwards. Occasionally, as a result of vascularization and organization of extruded disc tissue between the osteophytes, ossification may spread from one osteophyte to another, causing the radiological appearance of bony bridging.

It is not uncommon when studying X-rays of the lumbar and dorsal spine to find single, and occasionally double, lesions in an otherwise normal spine. It is probable that these isolated lesions represent the late result of traumatic rupture of the discs, rather than senile or pre-senile changes.

Incidence of Osteophytosis in Both Sexes at Various Ages

There are two methods by which the incidence of osteophytosis may be assessed, firstly by the study of the vertebral column at necropsy, secondly by radiography of the spine. The first method is the more satisfactory for obvious reasons, and a few such studies have been carried out, notably by Shore (1935).

The second method, namely radiography of the vertebral column, has certain limitations and disadvantages. Firstly, X-rays of the spine will only demonstrate osseous or calcified tissue, so that

cases which are in the stage where ossification of the osteophytes has not yet taken place will not be detected. Secondly, and for the same reason, the degree of the change may not be accurately assessed; and thirdly, a lateral osteophyte may not be seen in lateral views of the spine, nor may an anterior osteophyte be detected in antero-posterior views. Indeed, certain antero-lateral osteophytes may be missed in both views.

A recent review of the incidence of spinal osteophytosis has been carried out by Beresford (1952), who attempted to compare the incidence and degree of osteophytosis of the lumbar spine in Saskatchewan (Canada), and Bristol (England). He studied 1,922 X-rays taken for barium meals or enemata, intravenous pyelograms, cholecystograms, &c., excluding all films taken exclusively to show the lumbar spine. He does not state in what plane the spine was studied, but presumably his series consisted of antero-posterior views only. In addition, he assessed the degree of osteophytosis by comparing the length of the osteophytes with the breadth of the vertebral body. The objection to this method is that the vertebral body is roughly circular, and hence a true estimate of the ratio of the length of the osteophyte to the breadth of the vertebral body will only be gained when the osteophyte lies exactly parallel to the plane of the film. In all other planes, its position on the periphery of the circle will lead to foreshortening, and apparent reduction in its length.

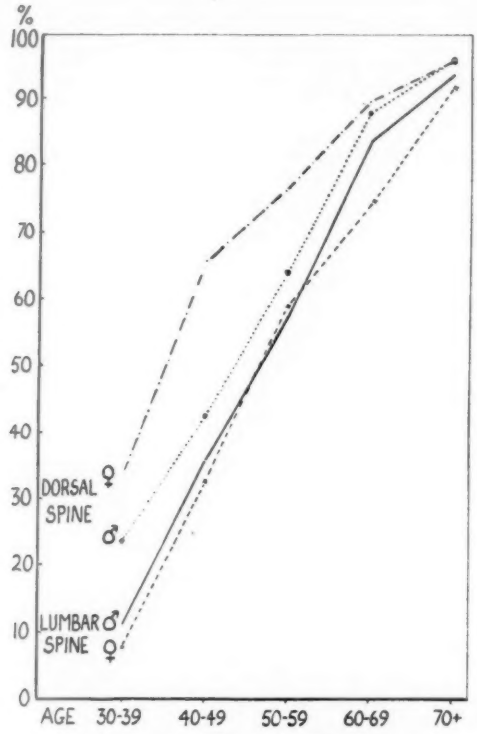


FIG. 1.—Age incidence of spondylosis.

In the present study, radiography has also been used in an attempt to assess and compare the incidence of spondylosis in the dorsal and lumbar spine in various age groups in both men and women. A total of 1,030 films have been studied, but in view of the difficulties already mentioned no attempt has been made to grade the degree of spondylosis, its presence or absence only being noted. For the lumbar spine, intravenous pyelograms, cholecystograms, barium meals and enemata, and straight views of the abdomen were studied, totalling in all 520 films. For the dorsal spine a series of 510 films were studied, made up of lateral or oblique views of the chest and barium swallows. In both groups, all films taken specifically to demonstrate the spine were excluded, as also were those films which showed only single or isolated double lesions in an otherwise normal spine, as it was felt that the latter might be due to traumatic rupture of the discs rather than to true degenerative processes.

Some of the disadvantages of this method have already been outlined. In addition, it must be borne in mind that patients in either group may have been suffering from pain of root or segmental distribution due to degenerative spinal disease, necessitating radiological investigation. In such cases the finding of spondylosis is not entirely fortuitous, and a false impression of the incidence may thereby have been gained.

Provided these disadvantages are borne in mind in assessing the results, they are not considered to be so serious as to invalidate the method.

Table I shows the result of this study in tabular form, and indicates the prevalence of spondylosis in the dorsal and lumbar spine of both men and women between the 4th and 8th decades. The fractions represent the number of patients with positive radiological findings over the total number studied in

TABLE I.—AGE INCIDENCE OF SPONDYLOSIS

	Lumbar spine		*Dorsal spine*	
	Male	Female	Male	Female
30–39 ..	6/56 (10·7%)	4/51 (7·8%)	12/50 (24%)	17/50 (34%)
40–49 ..	19/53 (36%)	17/52 (32·7%)	24/56 (42·9%)	33/50 (66%)
50–59 ..	30/52 (57·7%)	32/54 (59·3%)	32/50 (64%)	39/51 (76·5%)
60–69 ..	42/50 (84%)	39/52 (75%)	44/50 (88%)	46/51 (90%)
70+ ..	47/50 (94%)	46/50 (92%)	48/50 (96%)	50/52 (96·2%)
Totals	144/261 (55·2%)	138/259 (53%)	160/256 (62·5%)	185/254 (72·8%)

each decade, percentages being given in brackets beside each fraction. In the lumbar spine the figures for men and for women are similar, males showing a slightly greater incidence throughout. This difference is, however, small, and is not statistically significant. In the dorsal spine, however, the incidence of these changes is greater in both sexes than in the lumbar spine, and is significantly higher in each decade in women than in men. This finding is unexpected, and will be discussed later.

Fig. 1 represents these figures in graphic form, and suggests that if the investigation had been carried forward into the 9th decade, the four curves would meet. This suggests that spondylosis is a universal finding in those reaching 80 years of age.

Fig. 2 represents the distribution of these changes in the dorsal and lumbar spine of 200 patients of all ages. It will be noted from this that spondylosis most commonly affects the discs between the 7th and 11th dorsal vertebral bodies, and between the 3rd and 5th lumbar vertebral bodies. Between these areas, the incidence falls, as it also does at the lumbo-sacral junction. The significance of these changes in distribution will also be discussed later.

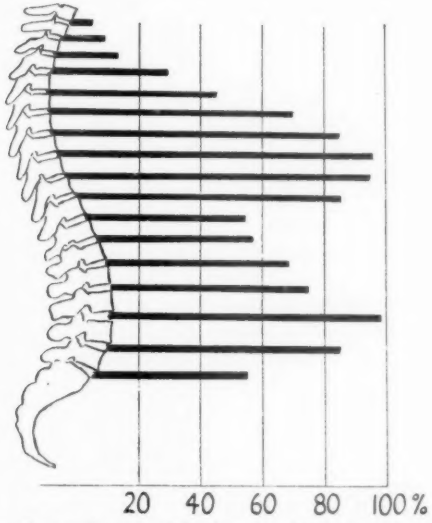


FIG. 2.—Distribution of osteophytosis of the dorsal and lumbar spine in 200 cases (all ages).

Discussion of Results

A. *Prevalence.*—Shore (1935) made a post-mortem study of osteophytosis of the spine, using "vertebral columns which had been macerated, dried, and rendered free from putrescible matter". Although he does not discuss the incidence of the condition in detail, he remarks that it is to be seen from the fourth decade onwards, and increases rapidly with advancing age. He goes on to say "I have never seen a vertebra bear osteophytes on the edge that is posterior and abuts on the spinal canal".

In the present study, the incidence of changes in the lumbar spine agrees fairly closely with reports from other writers. The frequency of changes in the dorsal spine, with a significantly higher incidence in women is not easy to explain. Among the factors which may play a part in the prevalence of spondylosis, the following demand consideration:

(i) Heredity. I have not been able to trace any studies on the effect of heredity in this condition. It seems possible that certain families may be prone to premature degeneration of their intervertebral discs, but a useful study of this factor would occupy many years before any definite conclusions could be reached.

(ii) Occupation. Although there is no convincing evidence to indict occupational stresses as a cause of spondylosis, our better understanding of the pathology of the condition makes it reasonable to suppose that those who bear heavy loads upon their backs, or are subject to flexion strains or excessive bending in the course of their occupation, would be more likely to develop these changes at an earlier age than their more protected fellow men. In this connexion one might be tempted to ascribe the occupational hazards of household duties as responsible for the predominance of changes in the female dorsal spine.

(iii) Obesity. This is another factor which deserves consideration, for the effect of obesity upon the articular cartilage of weight-bearing diarthrodial joints is well known.

(iv) Postural deformities. Many of the grossest examples of osteophytosis were seen in association with postural deformities of the spine. Nevertheless, it should be remembered that spondylosis itself will lead to exaggeration of the dorsal spine curve with consequent kyphosis, while, in the lumbar spine, it will tend to produce flattening of the lumbar curve, or even lumbar kyphosis. Other factors which may need to be considered are diet, climate, parity and trauma. A long-term study of these aspects of the problem will be necessary before any definite conclusions can be reached.

B. *Distribution.*—Shore writes:

"The liability of vertebræ to bear marginal osteophytes increases as the column is traced downwards. There are three well-defined 'outcrops'; (*a*) The cervical outcrop is marked off from the thoracic by a minimum zone at the junction of the first and second thoracic units. (*b*) The thoracic outcrop is higher than the cervical, and is separated from the lumbar outcrop by a diminution zone at the 12th thoracic vertebra. (*c*) The lumbar outcrop is higher than the thoracic, but falls to a minimum at the lumbo-sacral junction."

It will be seen that this description closely fits the findings in the present study. Shore explains the presence of these outcrops of osteophytosis by the intrinsic architecture of the vertebral column, which is arranged in three alternating antero-posterior curves. The junction points of these curves lie in the same vertical line with the line of gravity of the head and femoral heads, and it is at these points that the zones of diminution occur. At these points, the weight of the trunk falls vertically through the vertebræ, and there is a relative stasis of movement in relation to the posture and the ordinary movements of erect-standing man. On the other hand, the maximum changes are found at the zenith of the spinal curves, where movement is great, and where the weight of the body is transmitted obliquely through the vertebral bodies and intervertebral disc.

Although it is possible to agree with Shore's statement that the maximum changes are found at the zenith of the spinal curves, it is more difficult to accept the fact that there are "diminution zones" between these areas. It seems more likely that the maximum incidence of spondylosis occurs where movement of the spinal column is at its maximum and where the aggravating effects of postural deformities or occupational strains are at their greatest. "Diminution zones" are, in reality, areas thrown into relief by this heightened incidence.

We should, perhaps, not seek too far for a "cause" for spondylosis because we are most likely dealing with one of the natural changes in bodily tissues consequent upon advancing years, and the factors which have been considered may merely be aggravating influences upon an inevitable degenerative process.

REFERENCES

Bradford, O. D. (1952) *Ann. Rheum. Dis.*, **2**, 289.
Collins, D. H. (1949) The Pathology of Articular and Spinal Disease. London.
Coventry, M. B., Ghormley, R. K., and Kernohan, J. W. (1945) *J. Bone Jt. Surg.*, **28**, 233.
Keyes, D. C., and Compere, E. L. (1932) *J. Bone Jt. Surg.*, **14**, 879.
Pocock, A. (1952) *J. Anat. Lond.*, **86**, 162.
Shore, L. R. (1935) *Brit. J. Surg.*, **22**, 850.

Dr. Helen Dimsdale: *Neurological Significance of Cervical Spondylosis*

Cervical cord compression with radiological evidence of cervical osteoarthritis was described by Pastine as early as 1912. His patient developed a spastic paraplegia with inversion of the radial reflexes. X-ray examination of the cervical spine showed well-marked arthritic changes from C.3 to C.6 inclusive.

Elliott (1926) discussed the production of root compression by narrowing of the intervertebral foramina in cervical arthritis.

During the past three years the importance of cervical spondylosis as a cause of cervical cord syndromes has been recognised and its morbid anatomy described in a number of papers, notably by Epstein and Davidoff (1951) in America and by Brain *et al.* (1952) in this country. Brain (1948) was also responsible for distinguishing between the chronic disc protrusion of cervical spondylosis and the acute herniation of an intervertebral disc, frequently due to trauma, occurring in a previously radiologically normal spine.

Cervical spondylosis, due to the anatomical relationships of the intervertebral articulations has two chief neurological sequelæ which may occur separately or, less commonly, in association:

(1) *Radicular compression* due to narrowing of the intervertebral foramina.

(2) *Cervical cord compression* due to disc protrusion into the spinal canal.

(1) Radicular Compression

Mechanism.—The spinal roots emerging through the intervertebral foramen may be compressed anteriorly by osteophytes or soft-tissue swelling of the neurocentral joints, as described by Bull (1948). Arthritic changes in the articular joints constrict the foramen posteriorly. The vertical diameter is reduced by shrinkage of the intervertebral disc, with approximation of the superior and inferior borders. The anterior nerve root is also distorted by the lateral extension of the disc protrusion into the foramen.

Symptomatology and signs.—The onset of symptoms is not usually as acute, nor is muscular spasm as marked as in disc herniation. Intermittent aching pain develops in the muscles supplied by the affected roots, and is complained of in the neck, posterior scapula and pectoral regions, usually after an interval of some weeks, extending down the radial border of the forearm to the thumb, index and middle finger. The ulnar border is much less frequently affected, due to the relative sparing of C.7 and D.1 interspace from the spondylitic process. Intermittent paræsthesiæ occur in the periphery of the affected dermatomes, at first without objective sensory loss. If the pain has been present some weeks, slight loss to pin-prick and light touch appears on the radial border of the forearm, the thumb, index and middle finger, depending on the nerve roots affected. Proprioceptive sensibility is usually spared. The appropriate tendon-jerks are slightly reduced and minimal weakness with flabbiness of the muscles supplied by the affected roots becomes evident with, perhaps, some fasciculation. Occasionally the onset of symptoms and signs may be as acute as with a herniated disc lesion, and may follow trauma, exposure to cold or an infection. Perhaps swelling of the soft tissues of the intervertebral articulations is then the cause of the sudden onset of symptoms of root compression.

Adduction of the head towards the affected upper limb in cervical spondylosis is usually painful due to further reduction in the intervertebral foramen, in contrast to acute disc prolapse where resistance due to muscle spasm frequently makes abduction more painful. X-rays of the cervical spine show reduction of one or more disc spaces, disturbance of the normal cervical lordosis, arthritic changes in the neurocentral and articular joints, anterior, and, more important, posterior osteophytes. The root distribution of symptoms does not necessarily correspond with the narrowest intervertebral foramen, perhaps because dural adhesions or soft tissue swelling may be factors in the production of pressure.

Treatment.—Most patients with radicular compression due to spondylosis, improve rapidly with conservative treatment, such as rest, a plastic collar, and physiotherapy directed to improve the shoulder girdle muscles. Reduction of weight is also helpful.

Where there is clinical evidence of interference with sensory or motor function, unless improvement occurs rapidly with conservative treatment, a myelogram should be performed. The presence of any degree of block on examination of the cerebrospinal fluid, is also an indication for contrast radiography.

When a lateral disc protrusion or narrowing of the intervertebral foramen produces severe pain or focal signs, which do not respond to conservative treatment, the possibility of surgery must be considered. Occupational factors may also suggest the need for surgical treatment as in the following case:

A cartographer, aged 54, with a four-year history of recurrent pain and paræsthesiæ along the radial border of the right forearm, radiating to the thumb and index finger, found that the affected digits were becoming numb and weak so that he was unable to hold his pen. Examination showed loss of appreciation of pin-prick and light touch over the thumb and index finger, with slight reduction of the tendon-jerks in the arm. His cerebrospinal

fluid was normal in pressure and constituents. X-ray examination showed generalized degenerative changes affecting the neurocentral joints with lipping and osteophytic proliferation at C.4–5, and C.5–6. Myelography revealed a filling defect in the root sheath of C.6 on the right side. At operation Mr. Valentine Logue found that the sixth root bulged back over an immovable disc protrusion. Relief of symptoms was obtained by removal of the root of the lamina and decompression of the nerve. The patient has since continued his work as a cartographer.

(2) Cervical Cord Compression

Mechanism.—The degenerative changes in the cervical discs result in a proliferative response at the margins of the vertebral bodies. Posteriorly a large bar of fibrocartilage and osseous tissue is formed which projects centrally into the spinal canal, and impinges at its lateral extremities into the intervertebral foramina. The anterior aspect of the cord may actually be indented by one or more bars as shown by Brain and his co-workers (1952).

The posterior longitudinal ligament and the dura become thickened and adherent. Anterior compression of the cord results in traction on the attachments of the denticulate ligament to the transverse meridian of the cord, which Kahn (1947) has suggested produces the damage to the pyramidal tracts, so often present in spondylitic compression.

The anterior spinal artery may be intermittently occluded, especially on extension of the cervical spine when distortion of the cord is maximal, with resulting ischæmia of the anterior horn cells in the cervical and lumbar enlargement.

Symptomatology and signs.—Unless exacerbated by trauma, when an acute transverse lesion of the cord may occur, the neurological disorder due to cervical spondylosis is slowly progressive, usually over years. Clumsiness and tingling of the hands is complained of with weakness and unsteadiness of the legs. Symptoms of radicular compression may also be present.

The motor signs in the upper limbs consist of weakness, wasting and fasciculation which may be in the distribution of the compressed segments. However, wasting of the small muscles of the hand is not unusual when cord compression occurs at a higher segmental level.

The reflexes in the upper limbs may be increased due to compression of the pyramidal tracts by a disc protrusion above the cervical enlargement. The pyramidal lesion may, however, extend above the uppermost disc protrusion, due to traction on the cord. Reduction in the reflexes may occur as a result of segmental or root compression, and in the case of disc protrusion between C.4–C.5, which overlies the fifth cervical segment, inversion of the radial reflex may be found.

Cutaneous sensory loss in the upper limbs may be in a segmental distribution, or consist of slight peripheral blunting over the digits and hands, and sometimes a syringomyelic picture of dissociated sensory loss is found or a sensory level on the trunk. Proprioceptive sensory impairment occurs less frequently than cutaneous sensory loss. It has been suggested by Kahn (1947) that the posterior columns are spared by the denticulate ligament preventing posterior displacement of the cord. There is a spastic weakness of the legs of varying severity, often with little sensory involvement. Posterior column and cutaneous sensory loss may occur in the legs if compression of the cord is severe. Sphincter disturbances occur late.

X-rays of the cervical spine usually show an advanced degree of spondylosis, but cord compression may develop in the absence of marked changes in the straight X-rays, and the presence of disc protrusion may only be detected on myelography.

The cerebrospinal fluid frequently shows a small increase of protein with normal manometrics, rarely a block is present.

Diagnosis and treatment.—Cervical spondylosis most commonly produces damage to the cord in elderly patients, the protrusions are frequently multiple, and the clinical picture may be complicated by cerebral and spinal arteriosclerosis. Unless for some urgent reason such as a spinal block, surgery may be necessary, it is preferable to avoid myelography and to treat conservatively.

The recognition of spondylosis as a possible cause of cervical cord compression in the 4th, 5th and 6th decades is of great significance from the point of view of differential diagnosis and treatment. In these decades the history is usually shorter and damage to the cord less profound. Myelography is an important investigation to assess the significance of the X-ray appearances, and operative treatment may be indicated by the findings.

Signs of mid-line compression may result from a central protrusion, and a lateral protrusion may produce a complete Brown-Séquard syndrome or a partial one as in the following case:

A policeman aged 51, developed burning pains in his right foot at night and tingling in the left shoulder four and a half years ago, with progressive weakness of the left arm.

On examination there was wasting in the left upper arm, inversion of the left radial reflex, and signs of a pyramidal lesion in the lower limbs, left more than right. Examination of the cerebrospinal fluid showed a partial block with normal protein. The history of a fall off his bicycle shortly before the onset of symptoms five years earlier, suggested the possibility of cervical disc lesions, and gross disc degeneration from C.3 to C.6 was found on X-ray. Ultimately signs spread to the right arm. Myelography showed a defect extending from C.3 to C.6 when the contrast flowed on the left lateral aspect, with a constant defect at C.4–C.5.

At operation Mr. Valentine Logue exposed the right C.5 root and found it pushed laterally by an underlying disc protrusion against the outer margin of the intervertebral foramen. The bone of the margin was removed until the nerve seemed slack. On the left side the C.5 root was kinked laterally over a localized disc prolapse which was removed, and the nerve was decompressed. Wasting in the left upper limb remained, but the involvement of the right arm and incipient paraplegia was arrested.

Perhaps a more common problem than the recognition of cervical spondylosis as a cause of spinal compression, is its distinction from the virtually untreatable neurological disorders such as amyotrophic lateral sclerosis and disseminated sclerosis.

Tonic atrophy with fasciculation is common both to cervical spondylosis and amyotrophic lateral sclerosis. The clinical picture due to spondylosis may be recognised by some history of pain, the absence of involvement of the cranial nerves, the presence of sensory loss even if slight, some asymmetry of reflexes in the upper limbs due to root or segmental involvement.

The onset of root and cord symptoms due to cervical spondylosis may well suggest a diagnosis of disseminated sclerosis.

A stoker, aged 43, developed tingling of the anterior aspects of his thighs, and of the middle finger of both hands. In the course of a week his legs became heavy. There was no pain in the neck. The sensory symptoms were purely subjective. Tendon-jerks were slightly increased in the upper limbs, the lower abdominals were absent and he had a mild spastic paraplegia. He improved with rest, but as the paræsthesiæ persisted in the 3rd digits, and as straight X-rays showed gross disc degenerative changes at C.6–C.7, a myelogram was performed. This revealed mid-line obstructions at C.6–C.7 and above.

He has made a complete recovery with immobilization in a plastic collar and a change of occupation, although there may be a recurrence in later life. A central protrusion is not readily amenable to surgery.

To summarize, X-rays of the cervical spine including oblique views are advisable in patients with signs of a spinal cord lesion in whom the diagnosis is not obvious, to exclude cervical spondylosis.

A cerebrospinal fluid examination is necessary to detect any degree of block. Myelography is indicated to determine whether the changes detected on straight X-ray examination can be accepted as significant in the causation of the spinal cord lesion. Interference with the spinal canal by disc protrusions may be much more marked on myelography than the straight X-ray findings would suggest. It is preferable to avoid myelography in the elderly, infirm patient, in whose case surgical treatment is not likely to be advisable.

Rest in bed, a plastic collar for three to six months and attention to the neck and shoulder girdle muscles, is usually adequate initial treatment in cervical spondylosis. Where a cerebrospinal fluid block is present, or the pain and focal signs fail to respond to conservative treatment, neurosurgical advice should be sought, for surgical treatment is of great value in selected cases.

I should like to express my indebtedness to Mr. Valentine Logue for his operative findings

REFERENCES

BRAIN, W. R. (1948) *Proc. R. Soc. Med.*, **41**, 509.
——, NORTHFIELD, J., and WILKINSON, M. (1952) *Brain*, **75**, 187.
BULL, J. W. D. (1948) *Proc. R. Soc. Med.*, **41**, 513.
ELLIOTT, G. R. (1926) *J. Bone Jt. Surg.*, **8**, 42.
EPSTEIN, J. A., and DAVIDOFF, L. M. (1951) *Surg. Gynec. Obstet.*, **93**, 27.
KAHN, E. A. (1947) *J. Neurosurg.*, **4**, 191.
PASTINE, C. (1912) *Nouv. Iconogr. Salpêt.*, **25**, 405.

Section of Experimental Medicine and Therapeutics

President—G. A. H. BUTTLE, O.B.E., M.A., M.R.C.S., L.R.C.P.

[*October* 27, 1953]

DISCUSSION ON THE SURVIVAL OF TISSUES AT LOW TEMPERATURES

Dr. A. U. Smith (National Institute for Medical Research, Mill Hill, London, N.W.7): *The Use of Glycerol for Preservation of Living Cells at Low Temperatures.*

The majority of living cells, tissues and organisms are extremely sensitive to being frozen and thawed, both under natural conditions and in ordinary laboratory media. For this reason they do not survive when kept in the frozen state either at temperatures close to the freezing point of water, or at temperatures approaching the absolute zero, or in any intermediate range.

Some organisms, however, have forms which are resistant to adverse conditions; for example, spores of bacteria and moulds, seeds of plants and eggs of certain insects. These can withstand almost complete desiccation, and Becquerel (1932, 1950) showed that, in the dried state, they also survive freezing to and storage in liquid helium at −269°C. Luyet and his co-workers have shown that certain other cells, for instance frog spermatozoa and embryonic chick hearts, will survive freezing after partial dehydration in hypertonic solutions, and to a limited extent without preliminary dehydration, provided that they are cooled and afterwards rewarmed at an ultra-rapid rate (Luyet and Hodapp, 1938; Luyet and Gonzales, 1951). Luyet and his school believed that the preservation of life at low temperatures depended on preventing the formation of intracellular ice crystals, either by dehydrating the cells before freezing, or else by cooling and rewarming so rapidly that the protoplasm is converted to and from the vitreous state without formation of any crystals of ice (Luyet and Gehenio, 1940; Luyet, 1944). This theory, which has enjoyed great popularity, does not explain all the observed experimental data. Thus, a small number of lower organisms and a few types of cell from higher animals can be revived from very low temperatures without preliminary reduction of their water content, and after relatively slow cooling in ordinary media. Those of pathological interest include certain bacteria (Haines, 1938; Kyes and Potter, 1939) and a few species of pathogenic protozoa (Weinman and McAllister, 1947) and some kinds of tumour cells (Craigie, 1949; Passey and Dmochowski, 1950). The survival rate of these cells, however, appears to be low. Among isolated normal mammalian cells, human spermatozoa are exceptional, and Dr. Parkes (1945) has shown that a substantial proportion survive after untreated human semen is frozen by plunging ampoules or test tubes into solid CO_2 at −79° C. or into liquid nitrogen at −196° C., but none survive when microscopic amounts are frozen at the maximum rate.

Fragments of normal mammalian tissue cooled to very low temperatures at the maximum rate show excellent histological and cytological preservation (Gersh, 1932, 1952). Nevertheless, survival and multiplication of cells in cultures or grafts of rapidly frozen tissue has only been demonstrated conclusively with skin (Billingham and Medawar, 1952) and with thyroid tissue (Blumenthal and Walsh, 1950). The good functional results of grafting frozen and freeze-dried bone and artery are apparently due to hastened but orderly ingrowth of cells from the adjacent host tissues rather than to regeneration of cells within the implant (Pate, 1953; Rob and Eastcott, 1953; Hufnagel, 1953).

The special biological interest of studies on the effects of intense cold is the idea that, if a cell could be frozen to a very low temperature and thawed without damage, the length of time for which it remained frozen would be unimportant. In other words, at temperatures low enough to arrest bio-

chemical processes, the cell would remain indefinitely in a state of suspended animation. Until recently, however, even the shorter term practical project of preserving living cells at low temperatures for use a few weeks or months later seemed unattainable except in the few exceptional instances just mentioned.

The outlook was altered by an accidental discovery which we made four years ago at the National Institute for Medical Research (Polge *et al.*, 1949) that glycerol had the remarkable property of protecting the spermatozoa of the domestic cock against the otherwise fatal effects of freezing and thawing. This can be shown in a simple experiment. A sample of freshly collected fowl semen is diluted with an equal volume of Ringer's solution and the test tube frozen at −79° C. When it is thawed at + 40° C. none of the spermatozoa are motile, and all are distorted and dead. If, on the other hand, the semen is diluted with an equal volume of 30% glycerol in Ringer's solution and this sample, which contains a final concentration of 15% glycerol, is frozen at −79° C. and thawed at +40° C. in the same way as the glycerol-free control, the spermatozoa in the thawed material are fully motile and the activity in the sample differs in no way from that of the unfrozen control. In early experiments the glycerol appeared to have a harmful effect on the fertilizing capacity of the semen, and artificial insemination of glycerol-treated samples, whether they had been frozen or not, resulted in a negligible number of fertile eggs. Later experiments showed that the rapid removal of glycerol in the oviduct of the hen was the only source of damage, and that when the glycerol was removed by dialysis, before insemination of the frozen samples, their fertility was as good as that of unfrozen control samples (Polge, 1951). When these eggs hatched the chicks were normal in every way.

This showed that the spermatozoa were not only motile after freezing and thawing but possessed full functional capacity and that their genetic qualities were unaltered even after storage for many weeks in liquid air at −190° C.

Attention was then directed to the effects of glycerol and of low temperatures on mammalian semen. Bull spermatozoa were highly active after the semen had been diluted to contain 10% of glycerol. Artificial insemination of cattle showed that the semen had undiminished fertilizing capacity in the presence of glycerol, and that it was unnecessary to remove the glycerol before introducing the semen into the reproductive tract of the cow. Samples of glycerol-treated bull semen frozen by plunging tubes or ampoules into freezing mixtures at −79° C., however, contained very few actively motile spermatozoa when thawed. It was soon found that bull spermatozoa, which are sensitive to sudden temperature changes between + 37° C. and 0° C., were also sensitive to thermal shock between 0° and −79° C. Glycerol-treated bull semen which had been cooled slowly from 0° to −79° C. over the space of 30 to 40 minutes showed unimpaired motility when thawed and examined at body temperature. A technique was then worked out by Polge of diluting, cooling and long-term storage of bull semen at −79° C., for use at artificial insemination centres (Polge and Rowson, 1952*a* and *b*; Polge and Lovelock, 1952).

Large numbers of calves have now been produced as a result of insemination with glycerol-treated semen stored at −79° C. for long periods. There appears to be no deterioration in motility or fertility of bull semen during preservation for a year at this temperature.

Samples of glycerol-treated bull semen stored at −79° C. for 1–52 weeks gave an average conception rate of 65% when tested at four-weekly intervals in groups of 16 cows. The conception rate in cows artificially inseminated during the same period with freshly collected semen was 68%.

This method of preserving semen is now being applied not only in Great Britain but also in all the major cattle-breeding countries of Europe, America, Africa and Asia. It appears to promise economy in the number of bulls required for breeding, and to permit of progeny testing without wasting the most useful part of the bull's life, to facilitate the use of nominated sires and to make possible the global transport of semen.

Experiments on long-term preservation of mammalian eggs (Smith, 1952, 1953*a*) in glycerol-containing media at low temperatures have so far met with limited success as judged by the number of eggs which resumed normal division when cultured *in vitro* after thawing and removal of glycerol. It was noticed, however, that a high proportion of the ovarian follicular cells surrounding freshly shed rabbit eggs survived addition of glycerol and slow cooling to and storage at −79° C., and grew and multiplied in cultures. Experiments were therefore undertaken to determine whether ovarian tissue which had been exposed to very low temperatures *in vitro* would resume its normal functions of endocrine secretion and egg production when reintroduced into the animal body. Adult female rats were used for these studies, because in this animal the clear-cut cyclical changes in the cytology of the vaginal smear are suppressed by spaying and are restored by successful grafting of ovarian tissue. The ovaries removed from rats were treated with glycerol and frozen to and stored at −79° C. or −190° C. for periods varying from one hour to one year. They were then thawed and reimplanted subcutaneously. In some experiments the ovarian tissue was autografted into the animal from which it had been derived; in others it was homografted to another rat of the same strain or of a different strain. Vaginal smears were carried out daily on the recipients of grafts, and the interval before onset of œstrus was noted. The viability of frozen ovarian tissue was maintained even after storage in 15% glycerol at −190° C. for one year (Parkes and Smith, 1953), and the time of onset of

functional activity of the graft was little different whether it had been kept for one hour or for one year in liquid air at —190° C. Daily vaginal smears studied for months after implantation of frozen tissue, showed that œstrous cycles recurred regularly in a high proportion of the animals, and many of them mated at the time of œstrus (Parkes and Smith, 1953).

Histological studies have also been carried out to compare the regeneration of grafts from frozen and from unfrozen ovarian tissue. Although in frozen tissue the immediate degenerative changes are more severe than with fresh tissue, by the sixth day after grafting, regeneration of ovarian tissue is well advanced and young Graafian follicles or primordial follicles can be found in practically every section.

Between the 14th and the 28th day the sections contain many eggs in well-developed follicles as well as luteal tissue. At later stages, between 40 and 112 days after implantation of frozen tissue, the grafts seldom contain eggs and are composed of large areas of irregularly arranged luteal tissue as well as small collections of empty tubules. Nevertheless, vaginal cycles continue, as already mentioned, and many of the animals mate (Parkes and Smith, 1953).

Testicular tissue treated with glycerol has also given functional grafts after cooling to and storage at —79° and —190° C. Deanesly (1953) has found that homografts of infantile testes which had been kept frozen for many days became endocrinologically active when transplanted into castrated adults. When implanted subcutaneously into the loin spermatogenesis was incomplete, but when grafts were made into the scrotum all stages of spermatogenesis were seen, and at six to seven weeks the seminiferous tubules contained fully developed spermatozoa.

Grafting adrenal cortex into adrenalectomized animals is beset with difficulties, and assessment of results on the basis of survival of the recipients is complicated by the occasional occurrence of accessory adrenals which undergo compensatory hypertrophy in absence of the main glands. Nevertheless, glycerol-treated adrenal tissue has been frozen and thawed and grafted into adrenalectomized rats, and within four weeks a small proportion of the grafts have regenerated sufficient adrenal cortical tissue to keep the animals alive on a salt-free diet.

Anterior pituitary tissue also resists cooling to and storage at low temperatures provided that it is suspended in glycerol-containing media, as demonstrated in tissue cultures by my colleague Sydney Smith.

Portions of various mammalian organs and tissues other than endocrine glands have also been cooled to and kept at low temperatures in presence of glycerol and have regenerated when implanted into living animals. Among those which have survived are fallopian tube, uterus, vagina and seminal vesicle.

The use of glycerol-containing media has also enabled *Entamœba histolytica* to survive freezing and thawing and, for the first time, to remain viable during storage at —79° C. (Fulton and Smith, 1953).

So far each cell and tissue tested has required different treatment before revival has been demonstrated after freezing, low temperature storage and thawing.

One of the factors which influences the results is the composition of the medium into which the glycerol is incorporated. Other factors include the rate of addition of glycerol and the rate of cooling. Slow cooling is generally essential. Snap freezing or rapid freezing seldom gives good survivals. The storage temperature varies for different cells; for instance, bull sperm and rat testis survive long periods of storage at —79° C., whilst other cells and tissues, including fowl spermatozoa and rat ovaries, show a decrease in viability at —79° C. but can be stored for long periods without deterioration at —190° C. After thawing there is a tendency for frozen cells and tissue to deteriorate more quickly than is the case with freshly collected material. This is particularly noticeable with frozen ovarian tissue which loses viability during two hours at room temperature after thawing (Smith, 1953*b*).

Much work remains to be done in determining optimum conditions for preservation of different living tissue. Nevertheless the results obtained leave little doubt that, with the aid of glycerol, a wide variety of living cells and tissues could be stored for long periods at low temperatures for future use in experimental, diagnostic, or therapeutic medicine.

REFERENCES

Becquerel, P. (1932) *C.R. Acad. Sci., Paris*, **194**, 2158.

—— (1950) *C.R. Acad. Sci., Paris*, **231**, 1392.

Billingham, R. E., and Medawar, P. B. (1952) *J. exp. Biol.*, **29**, 454.

Blumenthal, H. T., and Walsh, L. B. (1950) *Proc. Soc. exp. Biol., N.Y.*, **73**, 62.

Craigie, J. (1949) *Brit. J. Cancer*, **3**, 268.

Deanesly, R. (1953) *Ciba Foundation Symposium*, Preservation of Normal Tissues for Transplantation. In press.

Fulton, J. D., and Smith, A. U. (1953) *Ann. trop. Med. Parasit.*, **47**, 240.

Gersch, I. (1932) *Anat. Rec.*, **53**, 309.

—— (1952) *in* Freezing and Drying: report of a Symposium held in June 1951. Ed. by R. J. C. Harris. Institute of Biology. London; p. 165.

HAINES, R. B. (1938) *Proc. Roy. Soc.*, B, **124**, 451.
HUFNAGEL, C. A. (1953) *Ciba Foundation Symposium*, Preservation of Normal Tissues for Transplantation. In press.
KYES, P., and POTTER, T. S. (1939) *J. infect. Dis.*, **64**, 123.
LUYET, B. J. (1944) *in* Colloid Chemistry. Ed. by J. Alexander. New York; Vol. 5, p. 859.
——, and GEHENIO, P. M. (1940) Life and Death at Low Temperatures (Monograph), *Biodynamica* Press, Normandy, Mo.
——, and GONZALES, F. (1951) *Biodynamica*, **7**, 61.
——, and HODAPP, E. L. (1938) *Proc. Soc. exp. Biol., N.Y.*, **39**, 433.
PARKES, A. S. (1945) *Brit. med. J.*, ii, 212.
—— (1953) Lecture on "Preservation of Living Cells", in Series "Scientific Basis of Medicine", Postgraduate Medical Federation. In press.
——, and SMITH, A. U. (1953) *Proc. Roy. Soc.*, B, **140**, 455.
PASSEY, R. D., and DMOCHOWSKI, L. (1950) *Brit. med. J.*, ii, 1129.
PATE, J. W. (1953) *Ciba Foundation Symposium*, Preservation of Normal Tissues for Transplantation. In press.
POLGE, C. (1951) *Nature, Lond.*, **167**, 949.
—— (1953) *Vet. Rec.*, **65**, 557.
——, and LOVELOCK, J. E. (1952) *Vet. Rec.*, **64**, 396.
——, and ROWSON, L. E. A. (1952*a*) *Nature, Lond.*, **169**, 626.
——, —— (1952*b*) *Vet. Rec.*, **64**, 851.
——, SMITH, A. U., and PARKES, A. S. (1949) *Nature, Lond.*, **164**, 666.
ROB, C. G., and EASTCOTT, H. H. G. (1953) *Ciba Foundation Symposium*, Preservation of Normal Tissues for Transplantation. In press.
SMITH, A. U. (1952) *Nature, Lond.*, **170**, 374.
—— (1953*a*) *Ciba Foundation Symposium*, Mammalian Germ Cells, p. 217.
—— (1953*b*) Effects of Low Temperatures on Living Cells. Chap. 1 in Freezing and Drying in Biology and Industry. Ed. by R. J. C. Harris. New York. In press.
WEINMAN, D., and MCALLISTER, J. (1947) *Amer. J. Hyg.*, **45**, 102.

Dr. J. E. Lovelock (National Institute for Medical Research, Mill Hill, London, N.W.7): ***Biophysical Aspects of the Freezing and Thawing of Living Cells.***

Three distinct lethal processes threaten the survival of living cells frozen and stored at low temperatures. The first is associated with the presence of ice crystals, both within the cell or throughout its suspending medium. The second is connected with the mere act of chilling, which, with sensitive cells, can cause death even at temperatures above 0° C. The third is a slow deterioration which takes place on storage at temperatures as low as −80° and possibly even at −180° C.

Most cells live in contact with a dilute aqueous medium and the effects of freezing are transmitted to them through this medium. In order to appreciate the stress applied to a cell it is helpful to consider how freezing takes place in a dilute aqueous solution. When a solution or suspension commences to freeze ice separates as a pure substance and the dissolved or suspended matter is concentrated in the fluid remaining between the ice crystals. The channels between the ice crystals remain continuous until almost all of the water has frozen. The continuity of these channels has been elegantly demonstrated by Dr. H. A. Sloviter (personal communication). He showed that when a suspension of red blood cells in glycerol saline is frozen to −15° C. and left for a few weeks the cells settle through the channels. The clear white supernatant and apparently solid mesh of ice crystals and the dark red sediment of blood cells, illustrate strikingly the freedom of movement still available to the cells at this low temperature.

When a suspension of living cells is frozen their first experience, apart from a drop in temperature, will be a crowding together and an increase in the concentration of their suspending medium. Crushing and spearing by ice crystals, if it takes place at all, can only occur later when the channels have shrunk to the same dimensions as those of the cells.

The response of a cell to freezing will depend at first, therefore, upon its reaction to an increase in the concentration of the suspending medium. If the cell is large and relatively impermeable to water, e.g. the fresh water amœba, the increase of osmotic pressure exerted by the suspending medium will have little influence on the concentration of its internal medium. As freezing progresses the cell will suffer supercooling and, eventually, usually between −5° and −10° C., will freeze internally. Chambers and Hale (1932) and Smith *et al.* (1951) have shown that this event is usually fatal. Cells which are highly permeable to water, most mammalian tissue cells for example, and cells which have a high surface to volume ratio, remain in osmotic equilibrium with their suspending medium during freezing. That is to say, they lose water as freezing progresses at a rate sufficient to maintain the freezing point of their inner contents at or only a little above that of their suspending fluid. By the time the medium has concentrated to saturation, at its eutectic, the cell will be too dry to freeze. There is, of course, no sharp distinction between these two types of behaviour. If the rate of freezing is very rapid internal ice crystals may form in small and water-permeable cells. Similarly, the large and relatively impermeable cells may be protected from the allegedly destructive effect of ice crystal formation by slow freezing.

Very few cells are capable of withstanding exposure to concentrated salt solutions; consequently most cells are irreversibly damaged long before their suspending medium has concentrated to saturation. It is found that −5° C. represents the lower limit to which mammalian cells can be frozen slowly without damage. At this temperature normal physiological suspending media would have concentrated nearly ten times. The destructive action of concentrated salt solutions is not instantaneous, and if cells can withstand very rapid freezing it is sometimes possible to preserve them for long periods at temperatures below −40° C. where all is solid. Thawing, of course, must also be rapid for successful survival.

Between 0 and −40° C. lies a critical region in which living cells perish if left in the frozen state for more than a few seconds. For cells which are permeable to water this region appears to coincide with a region in which the salt concentration exceeds a critical value for the cell; death on freezing is then a result of exposure to excessive salinity, and not, as sometimes suggested, to the mechanical effects of ice crystal formation (Luyet, 1949).

With cells which freeze internally—the fresh water amœba for example—it cannot be assumed that death results from mechanical disruption by the ice crystals however reasonable this may appear to be. When the cell freezes it suffers not only the mechanical intrusion of ice crystals but also the concentration of its intracellular electrolytes. There is so far no evidence to show which of these two effects is responsible for the death of the cell.

The first unequivocal demonstration that death on freezing resulted from exposure to strong salt was when Moran (1929) showed that the damage suffered by frog muscle could be explained quantitatively in terms of electrolyte concentration.

The nature of the destructive action of concentrated salt solutions appears to be connected with their ability to dissolve or disperse essential constituents of the cell membrane in particular lipids and lipoprotein. So far this feature of freezing damage has received systematic examination only with the red blood cell. With these cells (Lovelock, 1953*a*) sodium chloride solutions stronger than 0·8 M render the cell membrane cation-permeable. Hæmolysis then takes place either slowly in the strong solution or immediately when the cells are restored to isotonic media, as occurs when frozen cells are thawed. In salt solutions stronger than 2·0 M the structural integrity of the cell is destroyed.

It was discovered by Polge, Smith and Parkes (1949) that living cells could be frozen and thawed without harm if glycerol was included in their suspending medium. This discovery is of great practical value in the successful preservation of tissue at low temperatures and also provides important experimental evidence relevant to the general problem of freezing and thawing.

The effect of including glycerol in the medium used to suspend cells is to reduce the range of critical temperatures in which damage takes place. With human red blood cells it is found that as the glycerol concentration increases so the area of the critical region decreases until finally at a concentration greater than 2·5 M it vanishes. Closely similar results are obtained if other cells, for example spermatozoa, are frozen under the same experimental conditions.

It has been proposed that the critical region of temperature corresponds to a region in which the salt concentration of the cell and its medium are above a critical value for the cell in question. If this proposition is accepted it provides a simple explanation of the action of glycerol, namely that it functions as a "salt buffer".

Proof that glycerol does, in fact, protect cells against damage during freezing by functioning as a salt buffer is easy to obtain. If this function is assumed, it is possible to calculate from elementary physico-chemical principles the glycerol concentration needed to protect cells at various temperatures. The concentration of glycerol required in practice can then be compared with that required by theory. With the human red blood cell the observed and calculated glycerol concentrations differ by less than 3% (Lovelock, 1953*b*). Other cells subsequently examined show a similar close agreement.

The theory also requires that other non-toxic neutral solutes should protect cells against damage by freezing, and predicts the necessary concentrations. It was satisfactory, therefore, to find that many other neutral solutes including unlikely substances such as methanol and acetamide were able, at the required concentrations, to prevent the hæmolysis of red blood cells by freezing. None of the many substances tested was quite as effective as glycerol (Lovelock, 1954).

Living cells can enjoy the protection offered by neutral solutes only when permeated by them. There is no benefit in preventing the salt concentration of the medium outside the cell from increasing, if that of its interior is allowed to rise unchecked. This explains why larger molecules which do not permeate living cells, for example the sugars, are rarely successful in preventing damage by freezing.

The theory just described can offer some guidance in the practice of preserving cells in the frozen state. The chief practical contribution is the suggestion that freezing in the presence of glycerol may give even better results if the salt content of the suspending medium is reduced. This is particularly true with cells which normally live in a salt environment, for example sea water. The beneficial effects of reducing the salt concentration or of increasing the glycerol concentration of the suspending medium are additive. This suggestion may be of particular value when storage in the region between 0° and −4 °C. is contemplated. Chaplin and Mollison (1953) have shown this region of temperature to have

considerable potential value for the bulk storage of frozen cells, and to be convenient to maintain with conventional refrigeration equipment. It must not be forgotten, however, that for most cells the region 0 to −40°C. includes temperatures at which their destruction in the frozen state is most rapid.

The potential value of the physical interpretation of damage by freezing is likely to be greatest with cells whose preservation has not so far been attempted. With cells which have been subjected to preservation in the frozen state little improvement can be expected. The optimum conditions for their preservation have already been discovered with great skill and accuracy by the biologists (Parkes, 1953).

REFERENCES

CHAMBERS, R., and HALE, H. P. (1932) *Proc. Roy. Soc.*, B, **110**, 336.

CHAPLIN, H., Jr., and MOLLISON, P. L. (1953) *Lancet*, i, 215.

LOVELOCK, J. E. (1953*a*) *Biochim. biophys. Acta*, **10**, 414.

—— (1953*b*) *Biochim. biophys. Acta*, **11**, 28.

—— (1954) *Biochem. J.* In press.

LUYET, B. J. (1949) Preservation of the formed elements and of the proteins of the blood. *American Red Cross.*

MORAN, T. (1929) *Proc. Roy. Soc.*, B, **105**, 177.

PARKES, A. S. (1953) In press.

POLGE, C., SMITH, A. U., and PARKES, A. S. (1949) *Nature, Lond.*, **164**, 666.

SMITH, A. U., POLGE, C., and SMILES, J. (1951) *J. R. micr. Soc.*, **71**, 186.

Professor P. B. Medawar (Department of Zoology, University College, London): *The Storage of Living Skin.*

The storage of skin is an example of a technique that has been mastered before any important need for its clinical application has arisen. For at the present time all skin grafts must of immunological necessity be autografts, i.e. grafts transplanted from one part to another of a single individual. The storage of skin is therefore confined to the prudential act of setting aside a little spare skin at a first grafting operation in case it should be needed at a second. If it should ever become possible to transplant skin with permanent success between two different individuals, then skin banks would become commonplace. The use of skin homografts is at present mainly confined to the provision of temporary dressings to extensively burnt patients. The experience in the U.S. Naval Medical Centre[1] is that, used for such a purpose, the skin need not be alive; the skin to be grafted is therefore stored in the desiccated state. Skin and, for all we know to the contrary, other mammalian tissues are killed by desiccation (Billingham and Medawar, 1952). This paper will deal only with the storage of living skin.

The experiments described involve the removal of skin from the body and its storage in various ways for various lengths of time. In all such experiments the problem arises: how is the well-being of stored skin to be appraised? Histological examination is, in itself, inadequate, but several other possibilities suggest themselves. One may attempt to measure the degree of preservation of some "vital" function, like oxygen uptake or—as in Dr. N. Veall's unpublished experiments—the uptake of labelled phosphate. Alternatively the skin may be cultured for evidence of the outwandering of such cells as may still be alive. In Dr. Billingham's and my opinion, there is only one fully adequate method: to transplant the skin back to the animal from which it was originally removed. The criterion of fully successful storage is, quite simply, the restitution of skin to a state that is in every respect as good as new. Mere epithelial survival is necessary but by no means sufficient. Hairs and sebaceous glands must be formed anew; the melanocytes must persist and continue to endow the skin and hair with their natural pigmentation; and above all the collagenous endoskeleton of the graft must retain its integrity of fine structure. The transplantation test for survival is subject to one systematic error: by the act of transplantation, the skin is put through a further trial of its endurance, viz. survival through the extra two or three days that must pass before it is penetrated by blood vessels from its host. This imperfection is of no clinical importance whatsoever, for skin is stored only to be grafted, and storage will only be of value if the stored skin can take this last hurdle in its stride.

Storage at temperatures between 0° C. and body temperature.—Storage at body temperature, in an adequately nourishing and oxygenated medium, is, in effect, tissue culture, and skin banked in tissue culture enjoys the privilege of accumulating a certain amount of compound interest in the form of new-grown cells. The practical disadvantages of such a scheme are enormous; but it has the theoretical advantage that, by expanding the quantity of skin available for grafting, one is going some way towards solving the appalling problem of providing skin cover for patients so badly burnt as to be unable to provide sufficient sound skin of their own. Unfortunately, there are three good reasons for regarding this theoretical advantage as quite illusory: (*a*) The sheets of epithelium that may be grown in culture may certainly be grafted, but as grafts they are clinically inefficacious. Billingham and Reynolds (1952) have shown quite clearly that *mere* epithelial cover does not prevent the contracture of deep open

[1] *See* Storage of normal tissue grafts, *Nature, Lond.* (1953) **171**, 1047.

wounds, and also that if mere epithelial cover is all that is wanted it may be more easily provided by the direct grafting of a suspension of isolated epithelial cells. (*b*) Skin epithelium can in any event be grown more quickly on the patient himself than on his behalf *in vitro*, for the rate of epithelial outgrowth from pinch grafts or postage stamp grafts over granulation tissue is at least tenfold greater than that which can be achieved by explantation. (*c*) There is no reason to suppose that skin cultivated *in vitro* loses its antigenic specificity. It cannot therefore be used as a tissue homograft. If, on the other hand, skin homografts could be made to succeed, then tissue culture would at once become redundant, because sound skin, fresh or stored, from voluntary donors need never be in short supply. For completeness' sake, it may be added that mammalian skin can be stored in a state of temporarily suspended animation even at body temperature. Rabbit's skin epithelium, for example, will survive at least a week at body temperature in an atmosphere of hydrogen from which the last traces of oxygen have been catalytically removed (Medawar, 1947). Neither cellular division nor cellular movement can occur under these strictly anaerobic conditions.

Pepper (1954) has recently completed a study of the lifetime of rabbit's skin in *non-nutrient* media at temperatures ranging between 0° and 37° C. Her grafts were stored aseptically in sealed vessels upon a slip of filter paper damped with distilled water, and tested for survival by autoplastic transplantation, in accordance with the principles that have already been described. As was to be expected, survival time varies inversely with temperature, the maximal survival times of skin epithelium recorded at each temperature being as follows:

Temp. (°C.)	Survival time (days)
37	4
30	7
22	11
13	21
0	35

The maximal survival time at 0° C., five weeks, is surprisingly short. This may well be because, as Hanks and Wallace (1949) have already suggested, storage at zero is in fact inferior to storage at a slightly higher temperature. The curve relating survival time to temperature has a singularity in the neighbourhood of zero and the rule that survival time varies inversely with temperature is probably valid only for temperatures of +4° C. upwards. Pepper's findings are of some clinical interest because they strongly suggest that a thick skin graft would stand a better chance of surviving transplantation if its surface temperature were allowed to remain a little below 37° (Medawar, 1945, 1954).

Storage in *nutrient* media at temperatures above zero has been carefully investigated by Allgöwer and Blocker (1952); they find that split-thickness human skin grafts at 5° C. are better preserved in 10% serum than in saline-damped or vaselined gauze. Allgöwer and Blocker used both tissue-culture and transplantation tests of survival; in the main, the latter gave disappointing and inconsistent results. We must nevertheless insist that the transplantation test is as superior in principle as we have found it to be in practice. It is possible to imagine a storage system which gave superlative results when the stored skin was tested by tissue culture but which for some reason—e.g. swelling and "waterlogging" of the dermal ground substance—resulted in a graft that failed to take. Such a storage system would be clinically worthless. Skin is stored to be transplanted, and by its success in making transplantation possible a storage system must stand or fall.

Storage at temperatures below zero.—The work of Mider and Morton (1939) and of Briggs and Jund (1944) established the principle that mammalian skin epithelium withstands freezing to temperatures far below the eutectic point of normal saline. This work has recently been reviewed by Billingham (1953). Billingham's and my own research into the problem has already been published (1952), and beyond summarizing its results briefly we have only a few quantitative details to add.

In brief, skin is highly resistant to variations in the rate at which it is frozen, but ultra-rapid freezing such as may be secured by attaching a thin shaving of skin to a copper carrier and lowering it into a bath of isopentane chilled to −150° C. is fatal to its pigmentary cells. (The effect of the isopentane itself is negligible.) The impregnation of the skin shaving with 15% glycerol in Ringer's solution—a procedure in which we have followed the lead of Polge, Smith and Parkes (1949)—protects the pigmentary cells against the otherwise disastrous effects of ultra-rapid freezing. Glycerol itself appears to be entirely devoid of cytotoxic action in any pharmacological or chemical sense: even isolated epidermal cells will withstand a brief exposure to 98% glycerol, so that any ill-effects it may ultimately produce are probably due to osmotic dehydration.

Slow freezing is preferable to fast freezing by every standard against which the well-being of a graft can be measured. Even without a prior impregnation with glycerol, epidermal pigmentary cells—the most fragile constituent of skin—will survive slow freezing, a procedure which we achieve by the simple process of interposing an air jacket between the skin to be frozen and the solution which is to freeze it. This opinion is shared by all workers who have studied the freezing of skin, and by the

majority of those who have studied the preservation by freezing of any graft of the kind which has to be kept alive if it is to serve a useful purpose. There is a similar unanimity on the merits of quick thawing as opposed to slow. Skin epithelium, no matter how slowly frozen, can be killed by allowing it to rise slowly to 0° C. from the deep-frozen state; impregnation of the skin with glycerol before freezing will, to some extent, protect the epithelial cells against the evil consequences of slow thawing.

We do not yet know how long skin may be preserved at a temperature of −79° C. or below. Even the pigmentary cells of skin—as I have said, its most susceptible constituent—have so far contrived to live for 500 days at −79° C. when impregnated for 90 minutes with glycerol-Ringer immediately before freezing. It will occur to you that if the transplantation of skin back to its own donor is to be the test of survival, the donor will be a somewhat older animal at the end of such an experiment than at the beginning. Indeed, the figure I have just mentioned is taken from one of a steadily increasing number of trials in which we are removing skin from newborn rabbits, allowing the rabbits to grow up to varying stages of maturity and eventually of decrepitude and then returning the baby's skin to its own self, now adult. To anyone whose thoughts have turned towards a causal analysis of the mechanism of senescence, the import of these experiments is obvious.

REFERENCES

ALLGÖWER, M., and BLOCKER, T. G. (1952) *Tex. Rep. Biol. Med.*, **10**, 3.

BILLINGHAM, R. E. (1953) *Ciba Foundation Symposium*, Preservation of Normal Tissues for Transplantation. In press.

——, and MEDAWAR, P. B. (1952) *J. exp. Biol.*, **29**, 454.

——, and REYNOLDS, J. (1952) *Brit. J. plast. Surg.*, **5**, 25.

BRIGGS, R., and JUND, L. (1944) *Anat. Rec.*, **89**, 75.

HANKS, J. H., and WALLACE, R. E. (1949) *Proc. Soc. exp. Biol. N.Y.*, **71**, 196.

MEDAWAR, P. B. (1945) *Brit. med. Bull.*, **3**, 79.

—— (1947) *Quart. J. micr. Sci.*, **88**, 27.

—— (1954) *Proc. XVth Cong. int. Soc. Surg.* In press.

MIDER, G. B., and MORTON, J. J. (1939) *Amer. J. Cancer*, **35**, 502.

PEPPER, J. (1954) *Brit. J. plast. Surg.* In press.

POLGE, C., SMITH, A. U., and PARKES, A. S. (1949) *Nature, Lond.*, **164**, 666.

Dr. P. L. Mollison (From the Medical Research Council's Blood Transfusion Research Unit, Postgraduate Medical School of London): *The Preservation of Human Erythrocytes at Temperatures Below 0° C.*

One satisfactory feature of studying the preservation of red cells is that the objective can be precisely defined: the red cells should undergo no hæmolysis during storage and when transfused should survive in the recipient's circulation just as well as freshly drawn red cells. However, measurement of survival *in vivo* involves a considerable amount of work. For this reason investigators have frequently been tempted to confine their studies to changes occurring *in vitro* and to predict from these results the survival *in vivo*. Of the changes in red cells which can be studied *in vitro*, not one has yet been shown to be closely related to the maintenance of red cell viability, using the word viability to mean "ability to survive normally after transfusion". For example, a low rate of hæmolysis on storage does not imply that red cell viability is being maintained (Maizels, 1941; Mollison and Young, 1941, 1942). Changes in osmotic fragility are now clearly seen to depend largely on the osmolarity and composition of the medium in which the cells are stored: an increased resistance to hypotonic saline may be associated with diminished viability. Mechanical fragility is affected by factors, such as cell swelling, which are unrelated to viability. Chemical changes studied so far, such as the rate of dextrose utilization and of the release of inorganic phosphate, do not reflect the state of viability (Loutit *et al.* 1943). Thus, for the present, any claim to have found better methods of preserving red cells must be supported by the demonstration that the stored red cells survive well after transfusion.

Storage of red cells at temperatures above freezing point.—When blood is mixed with citrate-glucose and stored at +4° C. viability of the red cells is lost progressively with time; after one month's storage the blood is of little value as a source of viable erythrocytes. Adjustment of the pH of the medium to about 7·2 by the addition of citric acid greatly improves the maintenance of viability but after one month's storage, the post-transfusion survival of the erythrocytes is only about 70% as good as that of fresh cells (Loutit *et al.*, 1943; Gibson *et al.*, 1947; Ross *et al.*, 1947).

If blood is stored at room temperature even for as short a time as twenty-four hours, the post-transfusion survival of the erythrocytes is appreciably diminished (Ross *et al.*, 1947). This suggests that the loss of viability on storage is due to chemical changes which could perhaps be completely arrested if the temperature of storage were low enough.

Blood freezes at −3° C. so that until some method was found of protecting red cells against the otherwise fatal effects of freezing, −2° C. was the lowest temperature at which blood could be stored.

Storage at −2° C. has in fact been tried and found not to be appreciably better than storage at +4° C. (Chaplin *et al.*, 1953).

Storage of red cells in the frozen state.—Storage of red cells at temperatures well below 0° C. became possible when it was discovered that glycerol would protect living cells against damage by freezing (Polge *et al.*, 1949; Smith, 1950).

Sloviter (1951) showed that after red cells had been mixed with glycerol, frozen and thawed, the red cells could be freed from glycerol by dialysis and used for transfusion. Human red cells recovered in this way after having been kept at −79° C. for two hours survived normally in the recipient after transfusion (Mollison and Sloviter, 1951). In these experiments a solution of glycerol-saline was added to citrated blood from which part of the citrate-plasma had been removed. The final concentration of glycerol in the mixture was 18%. Blood stored at −79° C. with this mixture underwent progressive hæmolysis so that after six months only about 60% of the original number of red cells could be recovered for transfusion. However those red cells which were recovered survived normally after transfusion (Mollison *et al.*, 1952).

Blood stored with the same mixture at −15° C. to −20° C. hæmolysed more rapidly still so that after three months only about one-fifth of the red cells were left. Rather surprisingly these remaining red cells were also found to survive normally. It now appeared that −20° C. was a low enough temperature from the point of view of maintaining viability and it was presumed that if only the physical process causing progressive lysis could be interfered with, very satisfactory storage could be achieved. Experiments were therefore made to find conditions in which lysis would be much slower. Two main conclusions were reached. Firstly, that when blood was frozen in bulk—as in 500 ml. bottles—much less lysis occurred during freezing and thawing if the final glycerol concentration were in the range 20–30% rather than in lower concentrations. The rate of lysis on storage was also less when such glycerol concentrations were used. Secondly, it was observed that when red cells were mixed with sodium citrate and glycerol, rather than sodium chloride and glycerol, the rate of lysis during storage at −20° C. was enormously reduced so that after three months 98% of the red cells could be recovered (Chaplin and Mollison, 1953).

In view of the previous demonstration that red cells stored in saline-glycerol at −20° C. for three months survived normally, it was concluded that red cells stored in sodium citrate-glycerol were also certain to survive well after transfusion. It was rather puzzling that this proved not to be the case. However, on reviewing the details of the previous experiments it was realized that when using saline-glycerol a certain amount of plasma had been left with the red cells. In using the new citrate-glycerol mixture almost all the plasma was removed. Further experiments were therefore made in which more plasma was left with the red cells. It was now found that much better results were obtained; after three months' storage at −20° C. post-transfusion survival was about 90%. So far the conclusions are based on a relatively small number of observations and much more work must be done before we can be confident that we know which factors are associated with the maintenance of viability at −20° C. For example it is possible that the much better preservation observed when using the new plasma-citrate-glycerol mixture is due partly to the fact that the citrate content has been lowered, and not only to the fact that the plasma content has been increased. One reason for thinking that the presence of sufficient plasma may not be the only important factor in maintaining viability is the observation that in some experiments at −79° C. plasma has not regularly exerted this preservative effect (Chaplin *et al.*, 1953).

Whether −20° C. will prove to be a suitable temperature for storage for periods exceeding three months remains uncertain. We have shown that dextrose consumption by red cells is very slow at this temperature. Astonishing changes in cell electrolytes occur; for example, when the medium contains 3% trisodium citrate there is an almost complete loss of cell potassium which is only partially offset by an increase in cell sodium; however, these changes appear to be largely reversible *in vivo* (Chaplin *et al.*, 1953).

Methods of removing glycerol from red cells.—Whether this method of storage proves to be of any practical value depends to a large extent on whether a simple method of removing the glycerol can be devised. The glycerol can be removed by dialysis, by preliminary treatment of the cells with concentrated citrate or dextrose or sodium lactate, by washing the cells in falling concentrations of glycerol or by a continuous washing process. Dialysis was the first method to be used but has long since been rejected as being too clumsy. Lovelock (1952) introduced the method of exposing the red cells to hypertonic citrate to shrink them up and squeeze out most of the glycerol so that the cells could then be washed in normal saline to remove the rest of the glycerol. When this method was originally introduced red cells were being kept in 15% glycerol. However, when the use of 30% glycerol was introduced, it was found that treatment with 30% citrate did not remove enough of the glycerol so that considerable lysis occurred when the cells were exposed to saline. Moreover the red cells tended to adhere together and in re-suspending them much lysis occurred.

We have so far used the simple but tedious method of washing the red cells in falling concentrations of glycerol (16, 8, 4 and 2%) in 3% citrate: the red cells are then washed three times in saline. By such a process the glycerol concentration of a bottle can be reduced from 30% to about 0·05% and

relatively little lysis occurs. As this process takes four to five hours it will certainly be superseded by some continuous washing process.

Chaplin and Veall (1953) described a device for continuous washing, but the one designed by Brown and Hardin (1953) is probably better and we are at present experimenting with a model based on this design.

Whether or not this method of preserving red cells proves to be of practical value for transfusion, there is no doubt that it is very useful to blood group laboratories. Red cells stored in citrate-glycerol mixtures at −20° C. retain their blood grouping characteristics for at least six months although the reactions are usually a little weaker with cells stored for this length of time. It has, for example, proved extremely useful in our laboratory to store red cells of the rare genotype –D–/–D–. There is only one known donor of this genotype in England and it is obviously easier to thaw some red cells and wash them than to call the donor each time a small sample is required.

REFERENCES

BROWN, I., and HARDIN, H. (1953) *Arch. Surg.*, **66**, 267.

CHAPLIN, H., Jr., CRAWFORD, H., CUTBUSH, M., and MOLLISON, P. L. (1953) To be published.

——, and MOLLISON, P. L. (1953) *Lancet*, i, 215.

——, and VEALL, N. (1953) *Lancet*, i, 218.

GIBSON, J. G., EVANS, R. D., AUB, J. C., SACK, T., and PEACOCK, W. C. (1947) *J. clin. Invest.*, **26**, 715.

LOUTIT, J. F., MOLLISON, P. L., and YOUNG, I. M. (1943) *Quart. J. exp. Physiol.*, **32**, 138.

LOVELOCK, J. E. (1952) *Lancet*, i, 1238.

MAIZELS, M. (1941) Unpublished report to the Medical Research Council.

MOLLISON, P. L., and SLOVITER, H. A. (1951) *Lancet*, ii, 862.

——, ——, and CHAPLIN, H., Jr. (1952) *Lancet*, ii, 501.

——, and YOUNG, I. M. (1941) *Brit. med. J.*, ii, 797.

——, ——, (1942) *Quart. J. exp. Physiol.*, **31**, 359.

POLGE, C., SMITH, A. U., and PARKES, A. S. (1949) *Nature, Lond.*, **164**, 666.

ROSS, J. F., FINCH, C. A., PEACOCK, W. C., and SAMMONS, M. E. (1947) *J. clin. Invest.*, **26**, 687.

SLOVITER, H. A. (1951) *Lancet*, i, 823.

SMITH, A. U. (1950) *Lancet*, ii, 910.

Section of Epidemiology and Preventive Medicine

President—A. BRADFORD HILL, C.B.E., D.Sc.

[*October* 16, 1953]

The Epidemic of Poliomyelitis in Copenhagen, 1952

By H. C. A. LASSEN

Professor of Epidemiology, University of Copenhagen
Chief Physician Blegdam Hospital, Copenhagen, Denmark

DENMARK, like Sweden, has known poliomyelitis for quite a long time. We have had epidemics for as long as epidemic polio has been on record. The general trend in our country, as in other countries where epidemic polio has been established for decades, has been bigger epidemics, higher incidence of paralysis in the older age groups and a steadily increasing percentage of gravely-ill cases.

The metropolitan area of Copenhagen has a population of about 1,200,000 people served by a single hospital for communicable diseases, the Blegdam Hospital of 500 beds. During the last five months of 1952 we received about 3,000 patients with the diagnosis of poliomyelitis, roughly one-third with paralysis, two-thirds without. This, of course, was quite unusual but still more unusual was the high incidence of respiratory insufficiency with or without impairment of swallowing. Almost one-third of the paralysed patients belonged to this group.

At times we had 70 patients requiring artificial respiration; around New Year we still had 50 to 60 requiring it. To-day there are between 25 and 30 left over from the 1952 epidemic still dependent on artificial respiration.

The epidemic culminated about September 1. During the week August 28 to September 3 our hospital admitted 335 patients with polio or nearly 50 cases daily. And remember, about one-tenth of these patients were suffocating or drowning in their own secretions.

At our disposal we had one tank respirator (Emerson) and six cuirass respirators. This equipment naturally proved wholly insufficient when the epidemic got into its stride.

We had to improvise; we had to find ways of avoiding the impossible situation of having to choose which patient to treat in the available respirators and which patient not to treat. Every single patient should have his chance and an equal chance of survival.

In former years our therapeutic results in cases with respiratory insufficiency and involvement of the lower cranial nerves and the bulbar centres have always been very bad. During the eleven years 1934 to 1944 respirator treatment was used in 76 cases with a mean fatality rate of 80%. Only cuirass respirators were used. Fatality was 94% in respiratory paralysis with bulbar involvement and 28% in respiratory paralysis without bulbar involvement.

In 1948 we started to use tracheotomy in all cases where it proved impossible to maintain an open airway because of pooling of secretions and aspirations into the lungs. In the U.S.A. this procedure seems to have had a beneficial influence on prognosis. In our hands this has not been so. Thus the prognosis of poliomyelitis with respiratory insufficiency was rather gloomy at the outbreak of the 1952 epidemic in Copenhagen.

In the beginning of August when it became evident that an epidemic was imminent, one of my assistants, Dr. Lindahl with the aid of six senior medical students, was given the job of visiting the homes of all the polio patients. We drew up an extensive questionnaire including a host of questions. After eliminating all the doubtful cases about 2,300 cases of poliomyelitis remained—paralytic or non-paralytic.

Every seventh case of polio (316 in all) in chronological order was compared with an equal number of controls from the population. The polio and the control material were identical in age, sex and district. They were compared in a great many respects, in most of which no difference was found. Yet, in other respects, there *seemed* to be a difference, though this was not statistically significant. These concerned the incidence of head trauma inside one month before onset, the frequency of vaccination, intramuscular injections, the taking of blood samples, surgical intervention in the oropharynx, and pregnancy.

In a few points the difference was so conspicuous as to be highly significant statistically. This has to do with contagiousness.

TABLE I

CONTAGIOUSNESS I (Lindahl and co-workers)

Contact with polio	Poliomyelitis						Controls					
	Children		Adults		Total		Children		Adults		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Yes ..	64	28·4	25	27·5	89	28·2	12	5·4	1	1·1	13	4·1
No ..	161	71·6	66	72·5	227	71·8	211	94·6	92	98·9	303	95·9
	225	100	91	100	316	100	223	100	93	100	316	100

TABLE II

CONTAGIOUSNESS II (Lindahl and co-workers)

Contact with minor illness	Poliomyelitis						Controls					
	Children		Adults		Total		Children		Adults		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Yes ..	77	34·2	29	31·9	106	33·5	14	6·3	4	4·3	18	5·7
No ..	148	65·8	62	68·1	210	66·5	209	93·7	89	95·7	298	94·3
	225	100	91	100	316	100	223	100	93	100	316	100

About 60% of the patients had been in contact either with patients diagnosed as polio, or with patients having a minor illness. Only 9% in the control group come into this category. And, naturally, the control group chosen at random did include a few polio patients. These figures are strongly suggestive of the person-to-person contagiousness of poliomyelitis.

The intra-family contagiousness of the disease is also evident from Table III, which shows later cases of poliomyelitis or minor illness in the family *after* hospitalization of patient in poliomyelitis group.

TABLE III

CONTAGIOUSNESS III (Lindahl and co-workers)

	Poliomyelitis			Controls		
	Children %	Adults %	Total %	Children %	Adults %	Total %
Later cases of polio ..	8·4	5·5	7·6	1·3	0	0·9
Cases of minor illness ..	18·7	13·2	17·1	4·0	1·1	3·2
Polio or minor illness ..	26·2	18·7	24·1	5·4	1·1	4·1
Number	225	91	316	223	93	316

TREATMENT OF THE CRITICALLY ILL

I do not want to dramatize the state of affairs existing in the middle of August 1952, but it certainly was desperate ! Nearly all our patients with bulbar poliomyelitis had died!

On August 25 we decided to call into consultation our anæsthetist colleague, Dr. Bjørn Ibsen, as we thought positive pressure breathing—as used in modern anæsthesia—might be of value; and on August 27 the first patient received the treatment, which soon became our method of choice in patients with impairment of swallowing and reduced ventilation—a tracheotomy was performed just below the larynx and a rubber cuff-tube was inserted into the trachea with manual positive pressure ventilation from a rubber bag (bag-ventilation).

We were now in a position to treat every single patient requiring respiratory aid. In this manner we avoided being placed in the dreadful situation of having to choose. Patients kept pouring in, 30–40–50 a day, including 6–12 patients per day with respiratory insufficiency and/or impairment of swallowing—all of whom had to have special treatment. At the height of the epidemic the staff of doctors permanently on the job was 35–40; we had about 600 trained nurses and 250 medical students coming in daily, working in relays.

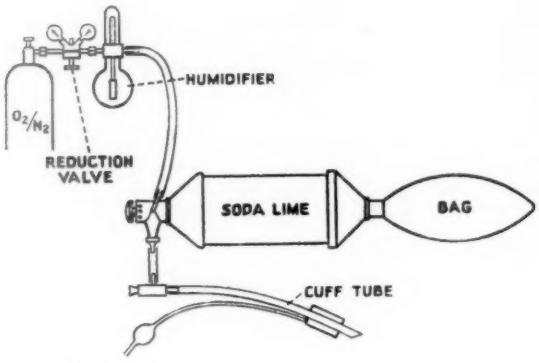


FIG. 1.

Fig. 1 shows schematically the various parts of the simple equipment used by us in about 200 patients subjected to manual bag ventilation. The upper part of the cuff-tube has a side branch connected with a metal container packed with granulated soda lime (Waters' canister) from which a rubber tube goes to a cylinder containing equal parts of compressed oxygen and nitrogen. A rubber bag is attached to one end of the canister, and a valve at the other end permits regulation of the pressure in the system. The cuff-tube is closed with a rubber stopper. If aspiration is needed, the stopper is removed and a Tiemann's catheter is introduced mounted on a jet suctioning apparatus. We have mostly used the ejector effect of a cylinder containing compressed air, which is very effective and is independent of electric power.

A good humidifier is essential, otherwise incrustation of secretions may occur.

In the acute phase several competing factors are involved, often difficult to diagnose and difficult to keep apart. These are: virus disease of the central nervous system; hypoxia; retention of carbon dioxide; and vasomotor shock.

In most cases one or more of these syndromes are present, the patients presenting a mixed clinical picture. Only careful clinical observation, supplemented by various biochemical tests, can guide us through this jungle of diagnostic difficulties and lead to a rational therapy. The clinical picture of these states is well known, I shall therefore only just mention that hypertension in patients with acute polio—especially bulbar polio—is not always due to hypercapnia. Some patients undoubtedly have hypertension due to central lesions, but this, of course, can only be ascertained after ruling out other ætiologies.

Our patients with respiratory insufficiency and/or impairment of deglutition have been treated in one or other of the four following ways, often in combination: (1) tracheotomy and positive pressure ventilation; (2) tracheotomy alone; (3) respirator—tank or cuirass; (4) postural drainage and permanent stomach tube.

The indications have been:

(1) For *tracheotomy and positive pressure ventilation:* accumulation of secretions in the upper airways, insufficiency of swallowing, ineffective cough, and a rapidly decreasing vital capacity.

(2) For *tracheotomy alone* eventually in combination with permanent stomach tube with continuous suctioning and postural drainage: pooling of secretions in the hypopharynx, paralysis of swallowing, ventilation normal or slightly to moderately decreased.

(3) For *respirator alone:* respiratory insufficiency without accumulation of secretions.

(4) For *postural drainage* often in combination with an indwelling stomach tube: impairment of swallowing without stagnation of secretion or slight accumulation of secretions and normal or slightly deficient respiration.

Following in the main these indications the great majority of our patients requiring special treatment had tracheotomy and bag ventilation. Very few patients could be tided over in respirators alone, either of the cuirass or the tank type.

I am quite aware that we may be under suspicion of having used tracheotomy and bag ventilation too freely. Yet, in 40% where tracheotomy and bag ventilation was the final therapeutic measure, treatment had begun with postural drainage or in a respirator. In all these cases we had to resort to tracheotomy and bag ventilation as a more radical therapy because of alarming symptoms of suffocation.

We soon came to the conclusion that in most acute cases it is impossible to differentiate between so-called central and peripheral respiratory insufficiency. The degree of the insufficiency was mainly estimated on a clinical basis. Practically all these patients had a feeble cough and inadequate or paradoxical respiratory movements.

In the more severe cases they also showed restlessness, disorientation, increasing blood pressure and cyanosis and, very often, accumulation of secretions in the airways and atelectasis.

An important point is the rate of progression of peripheral paralysis. If the upper extremities are involved, the temperature is high and the disease only a few days old, respiratory insufficiency will usually follow. Repeated measurement of the vital capacity has, in many cases, been of great help.

That our therapeutic principles have been fairly sound is, I think, borne out by the fact that our results steadily improved. Complications were very frequent (Table IV).

TABLE IV.—FREQUENCY OF COMPLICATIONS AND THEIR RELATION TO MORTALITY RATE

345 patients with respiratory insufficiency and/or impairment of swallowing. Mortality rate 41%

Complications	Frequency		Mortality rate	
	No. of patients	Per cent	No. of patients	Per cent
Shock	134	39	90	67
Paralytic ileus	114	33	49	43
Hyperpyrexia	66	19	60	91
Hypertension	65	19	27	42
Azotæmia*	36	22	28	78
Pulmonary œdema ..	28	8	26	93

*Adults only.

This table shows the incidence of the more important complications and their relationship to mortality rates. The mean mortality rate in the whole series was about 40%.

Vascular shock was very common especially in the first stage. It is often very difficult to pull these patients out of this state of vascular collapse, presumably because of lesions in the region of the medullary vasomotor centres.

Pulmonary œdema was quite common in the last phase of the disease. We saw it a few times after the removal of bronchial plugs, but the pathogenesis of this complication presumably most often was anoxic capillary lesions, myocardial damage and—a few times—too much intravenous fluid. Treatment was on the usual lines, but, as will be seen, it was not very effective.

Azotæmia of a very pronounced degree was quite common in these patients, probably because of increased decomposition of muscle protein. In some cases with impaired renal function on account of shock non-protein nitrogen values were especially high and the prognosis was very bad.

Hyperpyrexia, that is a temperature higher than 102° for more than five days after admission or until death, was not uncommon.

We do not know the pathogenesis of this pyrexia, but as it was present in many patients where an infectious origin was rather improbable, we felt it must be of central genesis. When this complication is present prognosis is almost invariably bad.

Certain complications such as *paralytic ileus*, *atonia of the stomach* and *arterial hypertension* were quite common but did not result in higher mortality rates.

After 26 August, 321 patients requiring special therapy were treated according to the principles I have already mentioned (Table V).

TABLE V

321 patients with respiratory insufficiency or with impairment of swallowing or with both (April 1, 1953)

	Men	Women	1–14 years	Below 1 year	Total
No. of patients	84	72	158	7	321
No. died	41	21	54	3	119
No. died (within 24 hours) ..	2	1	19	1	23
Mortality rate ..	49%	29%	34%		38%
Still artific. resp.	15	13	10	1	39
Spont. respt. trach. cannula ..	1	2	9	1	13
Spont. respt. cannula removed..	22	22	27	1	72

There was an equal number of children and adults. The percentage of adults is much higher than in the 2,300 patients with paralytic and non-paralytic polio. Of 321 patients 265—that is 82%—were treated with tracheotomy and of these, 232 had manual bag ventilation. The mean mortality rate was 39%. Adult women fared much better than adult men—29% against 49%. Why? we do not know.

Of the 119 who died, 23 patients died during the first 24 hours after admission, while 77 died during the first week. This gives an impression of the severity of the epidemic.

TABLE VI.—MORTALITY RATES

Group	Period of admission	No. of cases	No. died	Per cent
I	7/7 –25/8	31	27	87
II	26/8 – 8/9	50	27	54
III	8/9 –23/9	50	25	50
IV	23/9 – 5/10	50	20	40
V	6/10–21/10	50	13	26
VI	21/10– 6/11	50	18	36
VII	6/11–23/12	50	11	22
	Total II–VII	300	114	38

Table VI shows mortality rates in 331 patients requiring special treatment. First the group treated during the first month of the epidemic before bag ventilation was introduced: 87% died.

The next 6 groups each comprises 50 consecutive cases in chronological order without any omissions. The table shows that the mortality rate for these patients, of whom the great majority were treated by tracheotomy and bag ventilation, was reduced from over 80% to about 40%, representing about 120 lives. We are quite convinced that by far the greater number of these patients were saved by early tracheotomy combined with bag ventilation, and, further, that no mechanical respirator could have taken the place of the bag ventilation with equally good results. Here, too, the day of reference is April 1, 1953.

Observing the decreasing mortality rate during the course of the epidemic, we naturally searched for evidence of decreasing severity of the bulbar cases but could not find any, a clinical impression which is supported by the somewhat higher mortality rate in group VI.

Since the survey was made only comparatively few patients have died, up to date about 130 of a total of 350 requiring special treatment. 150–160 have been discharged with varying degrees of peripheral paralysis, yet, quite a fair number have only slight residual paralysis or no paralysis.

60–65 patients are still in the hospital and of these about 25 are still dependent on artificial respiration. Only very few of these unfortunates will ever regain enough spontaneous respiration to get rid of respiratory aid. In these patients ventilation had been mechanized in nearly all. Not one single patient is in a body respirator.

We do not think that this method is ideal, but we are still working at improving it. However, in comparison with the results formerly obtained in our hospital, it seems fair to regard the results as satisfactory in the circumstances.

The Anæsthetist's Viewpoint on the Treatment of Respiratory Complications in Poliomyelitis During the Epidemic in Copenhagen, 1952

By Dr. BJØRN IBSEN

Consultant Anæsthetist

Blegdam Hospital, Copenhagen, Denmark

On August 25, 1952, I was called in as anæsthetist for consultation by Professor Lassen in the Epidemiological Hospital of Copenhagen.

Within the preceding three weeks there had been 31 patients with bulbar poliomyelitis treated in respirators—tank as well as cuirass. 27 had died.

Four patients were seen in the autopsy room that day. One of them—a 12-year-old boy—had died in a respirator with a blood pressure of 160 and a bicarbonate level in the serum far above the normal level. The lungs did not appear to be sufficiently atelectatic to make adequate ventilation impossible.

With enthusiastic encouragement from Professor Lassen I tried to demonstrate on a patient how sufficient ventilation could be administered without the help of a respirator. A patient in a very bad condition was chosen. She was a 12-year-old girl who had paralysis of all four extremities. She had atelectasis of the left lung and was gasping for air and drowning in her own secretions. Her temperature was 40·2° C. She was cyanotic and sweating.

A tracheotomy was done immediately under local anæsthesia, and a cuffed endotracheal tube put in place through the tracheotomy. During this procedure she became unconscious. A to-and-fro absorption system was connected directly to the tube, with good endotracheal suction. Even then it was impossible to inflate the lungs, partly due to secretions and partly due to bronchospasm. In this desperate situation I gave her 100 mg. Pentothal i.v. in the hope that I could stop her struggling. She collapsed, her own respiration stopped and I found that I could now inflate her lungs.

Shortly after this a device for continuous measurement of the carbon-dioxide concentration in the air from one of the main bronchi—a Brinkman Carbovisor—and an Oximeter of the Millikan type, was put to work.

By these means it was shown how under-ventilation gave rise to a CO_2 accumulation—even when full oxygenation of the blood was maintained with pure oxygen.

The usual signs of CO_2 retention could now be demonstrated. There was a rise in blood pressure. The skin became clammy and sweating; and the patient started her own respiration, which soon became gagging and bucking—a well-known sign we had learned to recognize from some of the other patients seen in the respirators. Secretions began to pour out of the mouth and the nose. These symptoms could be relieved within a few minutes, when CO_2 was removed by increasing the ventilation.

Another important point could be seen in this patient. As soon as CO_2 was removed the blood pressure dropped to 80—and the patient appeared to be suffering from shock. Blood was given which improved her condition remarkably. She became warm, dry and pink—a condition which always makes an anæsthetist happy.

X-rays showed that the atelectatic left lung had been inflated completely.

So far, the patient had been improved by measures usually carried out by the anæsthetist during his daily work in the operating theatre: Active securing of free airway, adequate assisted ventilation and intravenous treatment of shock.

The patient was now put in a respirator. All the signs of under-ventilation occurred, and she once again got cyanotic. Administration of oxygen in the same way as to other patients in respirators revealed that her colour could be improved—and nearly full oxygenation ensured—but the Carbovisor showed a continuous rise in CO_2.

When the respiration was assisted in the respirator by intermittent squeezing of a bag connected with the tracheotomy tube, everything went well again. In this patient we had to continue the manually assisted respiration, because it was impossible for the respirator to maintain sufficient ventilation to secure the necessary elimination of CO_2. The reason was thought to be that the patient already had too many lung complications, thus making the respirator inefficient. The aim should be to protect the lungs against secretions, before the patient is put into a respirator. Our experience from a couple of late emergency tracheotomies, done under local anæsthesia, confirmed this.

The operation itself was difficult—performed on the bed or in a respirator. The patients were apprehensive and unco-operative probably due to anoxia. Bleeding into the lungs could not be avoided. During the handling of the trachea, anoxia was further aggravated due to spasm and reflexes. Finally some of the patients suffered from severe vomiting and aspiration during this procedure.

These emergency tracheotomies done late in the disease are almost useless. I do not remember many patients who survived a late procedure more than a few days.

Accordingly, it was felt necessary to have an endotracheal cuffed tube, which had been passed through the mouth, lying in the trachea before the tracheotomy could be performed. To accomplish this a general anæsthetic frequently had to be administered.

A free airway was thus maintained during the operation, and the respiration could be assisted as well, if needed. The surgeon had quiet operational conditions. The bleeding could be under control before the tracheotomy tube was inserted through the tracheotomy opening.

The first patient operated upon in this way, was found the next morning to have been seriously over-ventilated by the respirator during the night.

It was now possible to outline the principles of treatment:

(1) Any period of anoxia has to be avoided.

(2) When necessary a tracheotomy should be performed and a cuffed endotracheal tube inserted through the tracheotomy, in order to protect the lungs against secretions from above—allowing effective endotracheal suction—thus securing a free airway.

(3) The tracheotomy should be preceded by oral intubation. Most often this had to be done under general anæsthesia.

(4) Inadequate ventilation could be assisted when necessary by connecting the tracheotomy tube with a to-and-fro absorber system, and then manually performing an intermittent positive pressure ventilation. This method was suitable for patients actually in respirators as well as out of them.

(5) Shock should be treated with intravenous infusions—blood and serum, or vasopressor drugs, after the same principles as in surgical shock.

To carry out this treatment on all patients it was necessary to call upon additional staff. All available anæsthetists and medical students were mobilized and after eight days a big organization was working.

All patients with respiratory problems were collected in a special department, where they were under constant observation by a team, consisting of the epidemiologist, the ear, nose and throat surgeon, and the anæsthetist, all working with help from an excellent and capable laboratory. Later on radiologists and physiotherapists also helped.

There were in the department three floors, each with 35 patients, most of whom had their own room.

In order to secure continuity in treatment, conferences were held every day at which all problems were discussed. Specialists were invited to attend these conferences—physiologists, cardiologists, neurologists, &c.

Patients from the general wards—there were 500 beds, and 50 to 60 new cases coming every day—were transferred to the special department when they showed any of the following signs of respirator impairment: Difficulty in swallowing. Accumulation of secretions in the airway. A weak and insufficient cough, when the intercostal muscles or especially the diaphragm became paralysed. Paresis of the upper extremities. Progressive paresis moving upwards. Marked encephalitic signs.

A sudden vomit with aspiration could alter the situation in a few seconds, and make the use of the equipment necessary. A spare set of this equipment was kept ready on each floor, in case of failure of a patient's own set. This precaution has more than once proved to be life-saving.

Experience shows that the equipment to perform an artificial emergency respiration, and suction too, should be available within a reasonable time to every patient in respiratory trouble—even in his own home. During the polio epidemic, it became the principle, that this help should come to the patient, and not the patient to the help. Thus we went out by ambulance or by plane into the country, and rendered many patients capable of being transported.

In the observation department the patient's condition, and the indications for the different types of treatment, were evaluated. Patients were divided into wet and dry cases, according to the amount of secretion in the airway. They were also divided into a group, where the respiratory muscles seemed to be able to perform an adequate exchange when free airway was present, and a group who were thought not to be able to do so. The dry cases with sufficient ventilation, very few in number, were merely kept under observation. The dry cases with insufficient ventilation were most often put in a tank or cuirass respirator, in order to give them a chance to get through without a

tracheotomy. Only too often this was not possible. I remember only two patients who were put dry in a respirator, and remained dry. The wet cases who seemed to have sufficient muscle power to maintain an adequate exchange, were put in postural drainage. We tried to keep the airway free, but very often a tracheotomy had to be done, in order to maintain a free airway. This was especially the case in children, where there was little co-operation for suction and the drainage position was difficult to maintain.

The wet cases with insufficient ventilation had tracheotomy immediately, and were put on artificial respiration, usually administered through the tracheotomy tube.

As a rule we did not dare to put wet cases in respirators without a preceding tracheotomy. The few times we tried to do so we always regretted it.

In many cases where we were in doubt whether the impaired respiration was mainly due to secretions, or to decreased ventilatory muscle power, we did a tracheotomy. When the airway was made as free as possible, it was then decided whether the patient could be left in postural drainage, or had to have artificial respiration. Most patients had to have the latter.

The choice of anæsthesia for the tracheotomies was a difficult one. Pentothal and Scoline were used in the beginning, but were given up after one emergency, with cessation of the heartbeat of a patient in a tank respirator. I am not sure this was fair to the method. We got it started by heart massage and the patient improved but died the next night due to blocking of the tubes by secretions from a many days old complete atelectasis of the lung.

Later on cyclopropane was used. No premedication was given. Very often the patient stopped spontaneous breathing as soon as oxygen was given and had to be anæsthetized by squeezing the cyclopropane down into them.

A high tracheotomy was performed in order to stabilize the tube as much as possible in the trachea. A special device to maintain the tube in place was invented by one of the E.N.T. surgeons. The tube was changed when it was felt necessary. For practical reasons it was not possible to arrange a regular change. To our surprise, however, these rubber tubes gave rise to very little local irritation in the trachea.

The first hour after the tracheotomy was always very difficult. The reflexes might become exaggerated with the onset of pulmonary œdema. We were rather afraid of giving intravenous fluids during this time, before the tube was firmly in place.

The manual artificial respiration was done with a to-and-fro absorber system with a flow of 5 litres per minute and a mixture of 50% nitrogen and 50% oxygen. Since we had to use medical students, it was felt that this system had some buffer effect:

CO_2 excess could not develop if the absorber did not work.

Oxygen poisoning was not likely to occur.

Oxygen surplus was given to help in shock and pulmonary complications.

The high flow secured against low oxygen due to re-breathing.

There was no trouble with valves.

Drying out of the mucous membranes was probably not a problem as long as condensed water was present in the breathing bag.

Most of the patients had a stomach tube passed through the nose just after admission to the observation ward. The tube was left in place in patients who could not swallow, and used for giving food. Paralytic ileus was a common complication, which made the stomach tube a most valuable therapeutic measure in order to release the pressure on a weak diaphragm.

The cuffed rubber tube in the tracheotomy was replaced with a silver cannula as soon as possible. The E.N.T. surgeon decided when, by following the patient's capacity for swallowing. This we learned to respect. In some patients who were doing well on their own spontaneous respiration the chance was taken too early. The patients got atelectasis due to aspiration, and had to fall back into artificial respiration for weeks.

It was amazing, however, to see how the result could be improved by a very simple technique familiar to all anæsthetists. As soon as a patient is in trouble in a respirator he should—if the trouble cannot be corrected—have help by some other means. In Copenhagen it was artificial respiration through a cuffed tube inserted through a tracheotomy. The technique of performing this artificial respiration manually or mechanically can always be discussed and improved upon. But by the very simple technique used in Copenhagen, it was made possible, during the grave epidemic, to provide artificial respiration for every patient who needed it.